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A GUIDE

TO THE

CLINICAL EXAMINATION

OF

THE BLOOD

FOR DIAGNOSTIC PURPOSES

BY

RICHARD C. CABOT, M.D.

WITH COLORED PLATES AND ENGRAVINGS

Fifth Revised Edition

NEW YORK
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TO

WILLIAM SIDNEY THAYER, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE IN JOHNS
HOPKINS UNIVERSITY,

IN GRATEFUL RECOGNITION OF THE STANDARD OF THOROUGH
WORK ESTABLISHED BY HIM.

52897

PREFACE TO THE FIFTH EDITION.

About ninety pages of new matter have been added and about twenty pages stricken out. The most important changes are due to the introduction of the "Romanowsky" staining method (Jenner, Leishman, and others), as applied to routine blood examination. A new set of colored plates has been prepared from specimens stained in this way.

Considerable additions have been made to the chapters on Infectious Diseases and Blood Parasites and minor changes on almost every page in the book.

I am greatly indebted to Dr. Mary W. Rowley for her painstaking and, I think, most successful work upon the colored plates.

190 Marlboro Street, Boston,
April 1st, 1904.

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BOOK I.

INTRODUCTION.

SCOPE AND VALUE OF BLOOD EXAMINATION.

Hæmatology has now established for itself a definite field of usefulness in the practice of medicine. It has solved some problems where least was hoped from it, and given us disappointingly little help where great expectations had been aroused. We might have expected from it some light on the nature of rheumatism, furunculosis, uræmia, diabetes, but none has come.

On the other hand, who could have hoped that it would help us in the diagnosis of central pneumonia, of deep-seated suppurations, and of trichinosis, or in the prognosis of relapsing fever or of pneumonia?

There are probably not more than five or six diseases in which the blood examination gives us the diagnosis ready-made, but there is a very considerable number of conditions in which the blood examination will help us to make it. Not pathognomonic signs, but links in a chain of evidence are what we are to expect from blood examination. Very often the simple discovery that the blood is normal may be a fact of the greatest value in diagnosis.

On the whole it seems to me that the examination of the blood gives evidence similar in kind and not much inferior in value to that obtained by examination of the urine. Both methods of examination give us (*a*) a ready-made diagnosis in a few diseases; (*b*) side lights on a good many obscure conditions; and (*c*) the frequently great assistance of a negative report. In certain wards of the Massachusetts General Hospital it has been for some years the rule to examine the blood of every patient as a matter of routine at the time of entrance. In a small proportion of cases this gave negative evidence only; in a much larger proportion it materially assisted in the making of a diagnosis.

Improvements in technique have lessened the labor and increased the accuracy of blood examination. The most important facts about the blood of nearly every case can be obtained by a practised observer in fifteen minutes.

The blood is the only tissue that we can study easily during the life of the patient. Its relations to all other tissues are such that it is typical of them all in a way that no other tissue is, acting on all and being acted on by all. As yet we have studied chiefly its morphology, and from that single aspect obtained most of the clinically valuable information which we possess about it. But the field of the blood chemistry is in many respects even more promising at the present time, and there seems reason to believe that the study of the blood is still in its infancy and will take a higher place in the future as an aid to diagnosis, prognosis, and treatment.

Like all methods of physical examination it has especial usefulness when we cannot communicate with a patient, either by reason of his unconsciousness, stupidity, or insanity, or because he speaks no widely used language. In such cases the detection of marked anæmia, leucocytosis, eosinophilia, a typhoid serum reaction, or a malarial organism may be of great assistance. Malingering is made more difficult by it, and in the differentiation of organic from functional disease it is often very helpful. There is no febrile disease on which it may not throw light.

The evidence for these and many other aids furnished by the blood examination in clinical work is given in the later chapters of this work.

PART I.

METHODS OF CLINICAL EXAMINATION OF THE BLOOD.

CHAPTER I.

Confining ourselves to the clinically available processes by which we can gain information of diagnostic or prognostic value, blood examination at the present time embraces the following processes.

1. Estimation of the total volume of the blood and of its oxygen capacity.
2. Examination of the fresh blood (with or without a warm stage).
3. Counting the red and the white corpuscles.
4. Estimation of the amount of coloring matter.
5. Examination of dried and stained specimens.
6. Bacteriological examination of the blood.
7. Examination of the serum.[1]
8. Estimation of the coagulation time.

Less important are:

9. Estimation of volume of corpuscles and of plasma in a given quantity of blood.
10. Estimation of the specific gravity of the blood.
11. Estimation of the number of blood plates.
12. Estimation of the amount of fibrin.

To describe these processes in detail is the purpose of the next chapters.

I. Estimation of the Total Volume or Mass of Blood.

Until recent years the determination of the total mass of the blood has been practically beyond our reach, and our blood examinations have dealt wholly with small "samples" drawn from the periphery and treated as typical of the rest without regard to any possible variations in the total amount of blood in the vessels.

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[1] See Chapter xiii. of Book II.

But recently Haldane and Smith, in three important and interesting papers,[1] have suggested and applied a method which, if it stands the test of time and criticism, will add very materially to our knowledge of blood physiology and blood pathology.

The essential features of their method are as follows:

1. The patient inhales a measured volume of CO (a harmless and not unpleasant process). After two or three minutes a few drops of blood are taken for analysis and the percentage to which the hæmoglobin has become saturated with carbonic oxide is estimated (by the carmine method, see reference at foot of page).

2. Knowing the amount of CO inhaled, and the degree in which the blood has become saturated by this known amount, the quantity of CO capable of being taken up by the whole of that patient's blood can be calculated. Thus, supposing that the volume of carbonic oxide delivered was 150 c.c., and that the blood was twenty-five per cent saturated, it is obvious that the blood would have been one hundred per cent saturated by 600 c.c. Its total capacity for CO (or for oxygen) is 600 c.c.

3. How then shall we connect this estimate of total *oxygen capacity* with the *volume* of the blood? In a previous research the writers showed that the oxygen capacity per 100 c.c. of any given sample of blood can be accurately estimated by comparing its *color* with the color of an equal sample of *ox blood* whose capacity for oxygen has been previously determined. For example, a patient having absorbed 100 c.c. of CO, it is found that his blood is one-fifth saturated by this gas. The *total* capacity for CO (and so for oxygen) is therefore 500 c.c. But further, the patient's blood is found to have the same color as an ox's blood every 100 c.c. of which has been previously determined to be capable of taking up 20 c.c. of oxygen. The patient's total oxygen capacity (500 c.c.) divided by the oxygen capacity of every 100 c.c. of his blood (20) gives us 25. This figure is then the number of hundreds of cubic centimetres of blood in his body—2,500.

Smith has now applied this method to over one hundred cases, and found it to produce no appreciable ill-effects on the patient. As the result of these studies, he estimates the average volume of blood in health as 3,240 c.c. or 3,420 gm. The latter figure is obtained by means of the average specific gravity of normal blood (taken as 1.055). In the fourteen normal cases studied the blood mass varied from 2,830 to 4,550 gm. or $\frac{1}{30}$ to $\frac{1}{16}$ the body weight, but was never as large as had previously been estimated ($\frac{1}{13}$).

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[1] 1. Journal of Physiology, xxii., p. 232. 2. Journal of Physiology, xxv., p. 331. 3. Transactions of the Pathological Society, 1900, vol. li.

In chlorosis, Smith found that the apparent diminution in hæmoglobin was, in fact, due to the great increase in the plasma of the blood (serous plethora), the total oxygen capacity or hæmoglobin remaining normal. In pernicious anæmia, on the other hand, the amount of plasma is sometimes increased and sometimes diminished, but the oxygen capacity or hæmoglobin is always low. These observations will be referred to again later (see page 123).

II. Examination of the Fresh Blood.

(*a*) *Puncture.*—In all the processes about to be described (except the bacteriological examination) the first step is as follows:

Gently cleanse the lobe of the patient's ear with a damp cloth and then dry it. All vigorous rubbing or kneading is to be avoided. Attempts to sterilize the skin or to cleanse it with alcohol and ether are a waste of time. A small lancet or a bayonet-pointed surgical needle may be used; a sewing needle gives more pain and draws less blood from a given depth of puncture. A steel pen, with one nib broken off, makes a good lancet. The needle need not be sterile. In several thousand blood counts made at the Massachusetts General Hospital since 1893 the needles have never been sterilized and no signs of sepsis have been seen in any case.

Possibly this is due in part to the fact that the next step in the process after the puncture has been made is always to wipe away four or five successive drops as they emerge. This serves not only to get the blood flowing freely, but also to wash the ear in its own blood.

The puncture is best made into the lower surface or edge of the lobe, which is steadied with the fingers of the left hand. A very quick stroke gives least pain, the hand rebounding like a piano hammer. If the skin of the lobe is stretched tight with the fingers of the left hand so that no "give" is possible, the quick puncture gives hardly any pain. I have repeatedly taken blood from a sleeping child without waking it. What hurts the patient is the mistaken tenderness that slowly *presses* the needle through the skin.

The puncture must be deep enough to make the blood flow freely and without strong pressure, after it is once started by pressing out a few drops. Blood squeezed out with strong pressure should never be used for counting, as it may be considerably diluted with fluid from the neighboring tissues.[1] If the skin is moderately thin and the ear easily made hyperæmic, a puncture one-eighth of an inch deep is sufficient. With thick, bloodless skin it may be necessary to go in one-quarter or one-third of an inch—never more. *Beware of bleeders.* I have seen bleeding from a puncture made for a blood count which could not be checked for three-quarters of an hour. It is always safer to ask after a history of hæmophilia as a matter of routine before taking blood, just as one asks after false teeth before etherizing. If there is a history of hæmophilia, a mere touch of the needle point will give us all the blood we need without embarrassing us with a troublesome hemorrhage.

There is no question as to the superiority of the ear over the finger for drawing the drop. The ear is less sensitive than the finger, and a slighter puncture gives us all the blood we need. Moreover, it is a distinct advantage, especially in children, that the patient cannot watch the puncture of the ear, or the preparations for making it, and cannot easily withdraw the part. A sleeping patient often needs to be roused to get at his finger, while his ear is usually easily accessible above the bed clothes. Again, the absence of any bony prominence against which to press makes us less likely to use too much pressure than if we puncture the finger.

When one is making frequent examinations of the blood of a sensitive person, as in pneumonia, these details are of real importance, and in cases of pernicious anæmia in which the previous attempts to get blood from the finger had been absolute failures, I have found no difficulty in getting it from the ear. In this disease the advantages of the ear over the finger are peculiarly great.

Preparation of Temporary Specimens for Immediate Examination.

(*b*) When, after wiping away the first four or five drops, a good-sized drop exudes spontaneously, touch the centre of a perfectly clean cover-glass against the summit of the drop *without touching the skin itself at all*, and drop the cover-glass face downward upon a slide so that the force of the impact will help to spread the drop of blood thinly and evenly between slide and cover. It is recommended by Ehrlich and others to hold the cover-glass with forceps, but there is no harm in holding it with the fingers, provided we avoid touching either of its surfaces, *i e* , hold it always as in Fig 1[1]

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[1] Moderate pressure produces no error of importance.

Slide and cover must be perfectly clean, else the blood will not spread out in a layer thin enough to avoid the corpuscles overlying each other so that not one of them is clearly seen. Further, as dirt simulates fairly closely some of the pathological appearances for which we are on the lookout, its presence on the slide leads to loss of time or to mistaken conclusions. Cover-glasses, as they come from the shops, may be coated with a substance not easily to be removed. To get them really clean nothing is so simple as or more effective than soap and water. After several years' use of the method of cleaning usually advised (viz., strong mineral acid, followed by alcohol and then by ether), I have become converted to the use of plain soap and water as the best and simplest way of cleaning slides or cover-glasses. Rub soap over every part of the glass, wash it off with water, and polish thoroughly with a clean handkerchief (most towels are apt to leave a scrap of lint on the glass).[2] If slide and cover are perfectly clean, are held as in Fig. 1, and allowed to touch only the summit of the blood drop and not the skin, the blood will spread out properly between them, and no pressure on the cover-glass will be needed to make the layer of corpuscles thin enough. Pressure is undesirable, as it often makes all sorts of artefacts in the preparation and hastens crenation of the red corpuscles. Better results are obtained if slide and cover are *warmed* just before using, and it is well to have an assistant rub the slide vigorously with a towel just before it is used.

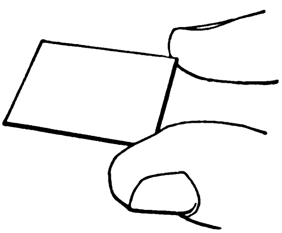

FIG. 1.—Proper Method of Holding a Cover-glass.

This method is, of course, applicable only to specimens to be immediately examined. Specimens which are to be transported or preserved should be prepared as directed on page 39.

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[1] I am not unmindful of Ehrlich's warning that the moisture of the fingers spoils the specimen; but in practice I do not find it to be true except as regards the margin of the film, the good preservation of which is not essential. Only the thinnest cover-glasses in the market should be used, ⅞ inch is the best size.

[2] Further experience has convinced me that water alone is generally sufficient, provided the polishing, which is the chief factor of success, is thorough. Tissue paper is very useful for polishing cover-glasses. After polishing, it is well to pass them through a Bunsen or alcohol flame once or twice.

Prevention of Cell-Death.

Slides so prepared are usually best examined with a one-twelfth oil-immersion lens. As a rule they keep long enough for purposes of examination without any further precautions, but if we desire to keep the blood fresh and uncoagulated for a longer period, it is best to exclude air in this way: Paint upon the slide with vaseline, cedar oil, or any gummy substance a hollow square or ring of about the size of the cover-glass, so that when the latter with its drop of blood is put down upon the slide the drop will spread out inside the ring of oil, which seals the margins of the cover-glass to the slide. Specimens so prepared will keep for many hours unchanged, and without crenation or coagulation, if the weather is warm or if the slide be kept in a warm place.

In examining blood suspected of containing malarial parasites it is sometimes useful to put the whole microscope into one of the warming apparatuses devised for the purpose. This is better than any of the various kinds of warm stage in use; but in clinical work there is rarely if ever any need for artificial heating apparatus of any kind, provided the room and the slide are warm.

What Can be Learned from Fresh Blood.

In the first place we note the readiness or sluggishness of its flow from a puncture of standard depth. The blood flows more readily than usual in the following conditions:

1 Peripheral congestion or vaso-dilatation.

2 Exaggerated fluidity of the blood (chlorosis, some types of anæmia, and hæmophilia).

It flows sluggishly:

1. After profuse hemorrhage or serous drain (cholera).

2. In certain cases of extreme anæmia—*e g*, emaciated cancer cases.

3. Vasomotor spasm (cold, hysteria, Raynaud's disease, uræmia —certain cases).

4. Exaggerated coagulability

Examination of the fresh blood by the method described above is also a good way for ascertaining the presence or absence of—

1. The Plasmodium malariæ
2. The Spirochæte of relapsing fever
3. The Filaria sanguinis hominis and the Trypanosoma.
4. Rouleaux formation among the red cells.

It is also a quick and convenient method of finding out with approximate accuracy:

(*a*) Whether the blood contains an increased amount of fibrin;

(*b*) Whether any considerable anæmia or leucocytosis[1] is present;

(*c*) Whether or not the amount of hæmoglobin in the red cells is much decreased;

(*d*) Whether the red corpuscles are deformed;

(*e*) Whether the "blood plates" are increased or not. A practised observer can also make a diagnosis of leukæmia by this method in most cases, but here mistakes may easily occur.

So much can sometimes be learned from a specimen prepared in this very quick and easy way that it should be as much a matter of routine as a urine examination. But in order to get any information from such a preparation we must previously have familiarized ourselves with the appearance of normal blood under such conditions—with the size, shape, color, and refractions of the red cells, white cells, and blood plates and their ratio to one another, and with the great variety of curious phenomena to be seen as a drop of blood gradually dries up between slide and cover. No book can teach this; it must be learned by actual experiment.

Some of the commoner sources of error will be referred to later. Here I will mention only the Brownian movement in the protoplasm of the corpuscles, to be distinguished clearly both from the amœboid movements of the leucocytes or of the malarial parasite and also from the irregular contractions of the dying protoplasm, which give rise to pseudo-amœboid motions in the crenated points of normal red cells or in the irregular projections of corpuscles deformed by disease (*vide infra*).

For a more detailed description of normal red corpuscles, white corpuscles, and blood plates the reader is referred to Part II.

An account of the pathological changes to be observed in the fresh blood will be given in later chapters.

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[1] More accurately it is only the ratio of red to white corpuscles that we can determine, and when the red are very much diminished in number we may be deceived into supposing that the white are increased.

CHAPTER II.

COUNTING THE CORPUSCLES.

I. The Thoma-Zeiss counter.

II. Durham's modified counter.

I. Out of the many instruments devised for this purpose that of *Thoma-Zeiss* with Zappert's modified ruling of the counting chamber is the best, and much the most commonly used.[1] In the use of this instrument there are five steps or stages:

1. Puncturing the ear.
2. Diluting and mixing the blood thus obtained.
3. Adjusting a drop of diluted blood in the counting chamber.
4. Counting the corpuscles.
5. Cleaning the pipette.

To count the white corpuscles, an instrument different from that employed for the red is often used.

The technique is nearly the same for both instruments, but for clearness' sake I shall describe them separately. To save time I shall call the small-bore pipette used for red corpuscles (Fig. 2, *A*) the "red counter," and the large-bore pipette (Fig. 2, *B*) the "white counter."

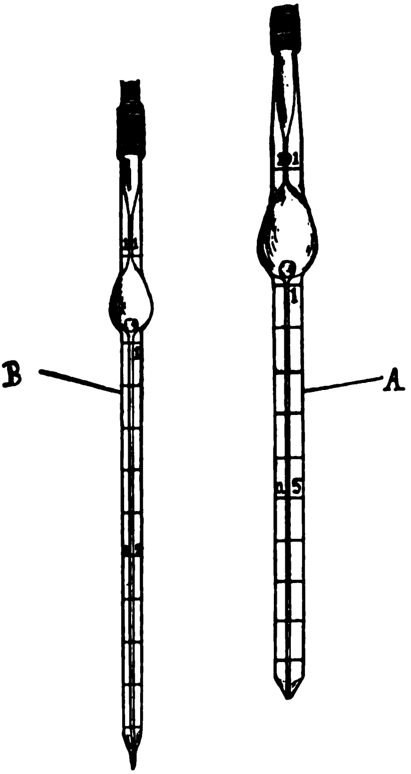

Fig. 2.—Thoma-Zeiss Pipettes. *A*. For red corpuscles; *B*, for white corpuscles.

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[1] The various modifications introduced from time to time do not seem to me to present advantages sufficient to make them deserve to displace the original instrument.

Counting the Red Corpuscles.

(*a*) After puncturing the ear as above described, and as soon as the blood is flowing freely, put the point of the "red counter" into the drop as it emerges from the ear, and by sucking gently on the rubber tube attached to the other end, draw up blood to the mark 0.5 on the pipette. It is convenient to rest the end of the pipette on the thumb as shown in Fig. 3. It needs some practice to stop exactly at the mark, but if we happen to draw the blood up *a little* past the mark 0.5 no considerable error results, provided we draw the column down again to the mark by tapping the point of the pipette on a towel, and provided also that the instrument is perfectly clean and dry. The aim and intention, however, should always be to stop exactly at the mark 0.5, and with a little practice we can do it, except with nervous or delirious patients, and those who carelessly move the head just at the critical moment. With such patients we usually have to content ourselves with drawing the blood a little beyond the mark 0.5 and then drawing it down again to the mark as above described.

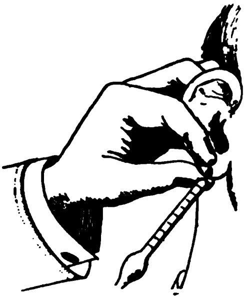

FIG. 3.—Method of Resting Point of Pipette on the Thumb while Sucking in Blood.

Diluting the Blood.

(*b*) The bottle of solution to be used for diluting the blood should be ready uncorked at the bedside. Of the many solutions suggested by various authors none is better than *Gower's*, the formula for which is as follows:

Sodii sulphat	gr. 112
Acid. acet	ʒ v.
Aquæ	℥ iv.

Toisson's solution is also very useful and stains the white corpuscles so that they can be easily distinguished from the red. Its composition is as follows:

Methyl violet, 5 B.	0.025 gm.
Sod. chlor	1.000 "
Sod. sulph	8.000 "
Neutral glycerin	30.000 cm.
Aquæ destill	160.000 "

We must wait about ten minutes after mixing before the leucocytes are fully stained. Except for this delay, the only objection to this solution is that it is rather difficult to clean the pipette after using it. If the white cells are counted with another pipette the staining fluid can be as well dispensed with.

Into a bottle of one of these solutions, ready at the bedside, the point of the pipette is to be plunged as soon as the blood has been drawn up to the point 0.5 and the outside of the pipette wiped clean of blood. Suction is then exerted through the rubber tube *the instant* the point of the pipette is below the surface of the diluting solution. This suction is continued until the diluted blood has filled the bulb of the pipette and gone past it up to the point marked 101. It is not difficult to stop at this point, provided the pipette is perfectly clean and dry inside. Otherwise it is impossible. Should any mishap occur at this point, the whole process must be begun over again after carefully cleaning and drying the pipette. If no accident happens and the mixture is sucked up to and not past the mark 101, we have diluted the blood with two hundred times its bulk of neutral solution. If, instead of drawing the blood up to the mark 0.5, we draw it as far as the point marked 1, and then dilute as above described, the mixture will be 1 to 100. Some observers habitually use this dilution. The objections to it are (1) That if the blood is accidentally drawn up too far (*i.e.*, past the mark 1) we cannot draw it down again but must painfully clean and dry out the pipette (see page 18) and repeat the process. (2) If the blood contain approximately the normal number of corpuscles, they will be so crowded when adjusted on the ruled surface of the disc A that it is more difficult to count them. If we use another pipette for the white corpuscles, the dilution of 1:100 has no advantage to counterbalance these drawbacks.

While sucking in the diluting solution, it is well to roll the pipette on the long axis with the fingers of the hand which holds it in the diluting fluid. This mixes the blood instantly and prevents any of it from floating on the top of the solution and thereby coming up undiluted into the narrow portion above the bulb of the pipette, where it might possibly escape thorough mixing.[1]

Next we thoroughly mix the blood and diluting fluid by shaking and rolling the pipette, its ends being closed by the fingers. The little glass ball within the bulb helps this process materially. A minute's brisk rolling and shaking is as good as five minutes', as I have convinced myself by many experiments, and the distribution of the corpuscles throughout the mixture is very even, provided there is no delay in proceeding to the next step,[1] viz.:

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[1] Care must be taken that no saliva finds its way through the rubber tube and into the pipette. Never blow through the rubber tube.

(*c*) *Adjusting a Drop of Diluted Blood in the Counting Chamber.*—Remove the rubber tube from the pipette and blow out the portion of diluting solution which *last entered* the pipette, and which consequently has not been thoroughly mixed with the blood in the bulb. Five or six drops should be blown out before any is used for examination. Next, put upon the surface of the counter (A, Fig. 4) a drop of such size that when the cover-glass (B) is let down over it, the whole of the disc A is covered with the drop without any being spilled into the "moat" (C) around it. Just how large such a drop should be, can be learned only by practice. It is not literally necessary that exactly the whole disc A should be covered, provided nine-tenths of it is covered, but any spilling over into the "moat" (C) entails serious error.[2]

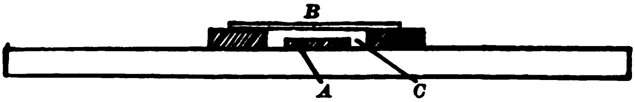

FIG. 4.—Thoma-Zeiss Counting Slide. *A*, Ruled disc; *B*, cover-glass; *C*, moat.

After the cover-glass has been let down upon the drop, we should be able (provided the whole instrument is *clean*) to see concentric rainbow rings between the cover-glass and the body of the instrument. These are known as Newton's rings. A little pressure with a needle on the cover-glass will often bring them out if they do not at once appear, *but they must remain visible* after the pressure is taken off. Otherwise we know that there must be some dirt or dust under the cover-glass preventing its settling exactly into position, and this will cause error in the count, though not a very considerable error in most cases. (To see Newton's rings we should get our eyes near to the level of the counting chamber so that the light from window or lamp is reflected from the surface of the cover-glass.)

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[1] If we have to pause before going on to the next step, we must take care to roll and shake the pipette again when ready to proceed.

[2] In accordance with Meissen's suggestion Zeiss now supplies this apparatus with a groove in the glass disc outside the "moat," whereby communication is established between the latter and the external air. Thus the results of counting are made independent of differences in atmospheric pressure.

If the above conditions are not all fulfilled, the instrument should be washed and another drop tried, after shaking the pipette and blowing out a few drops as before.

The cover-glass must be let down as soon as possible after the drop has been put on the disc A, and before the corpuscles have time to settle. It is best to let it down with a needle as in mounting microscopic specimens.

Counting.

(*d*) After waiting two or three minutes so that the corpuscles may settle thoroughly upon the space ruled off on the disc A, "the whole blood-covered area of the ruled slide should be examined first by low power, and, no matter what distribution obtains over the ruled square, if over the whole field the cells are not quite uniformly distributed, the slide should be cleaned up and another drop examined" (Emerson).

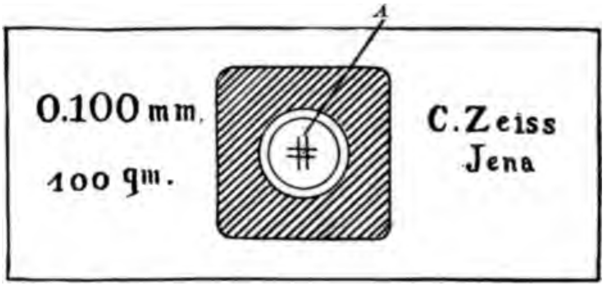

FIG. 5.—Thoma-Zeiss Counting Slide. *A*, Ruled disc.

If the distribution seems everywhere uniform, the counting is begun, using preferably an objective 5 of Leitz or D of Zeiss and a No. 1 or 2 eyepiece.

The central part of the ruled space on the surface of Zappert's counting chamber (A, Fig. 5) is divided into four hundred squares, every group of sixteen squares being enclosed in double lines to make it easier to know how many squares we have counted (see Fig. 6). Including the squares with double lines we have a group containing thirty-six small squares, a group convenient to count at one time as it just about fills the field of the objective Leitz No. 5, or Zeiss D with a No. 2 eyepiece.

To avoid considerable error we should count the corpuscles in five fields of thirty-six squares each, such as is shown in Fig. 6, taking the fields in various parts of the whole ruled space. The instrument should then be washed[1] and the whole process repeated with a second drop. If the count of the second drop differs widely from that of the first, a third drop should be counted, and the average taken of those two which are most nearly alike. Thus at least three hundred and sixty small squares should be counted; with such a number the error is not over three per cent for practised observers.[2] In normal blood this means counting about 2,160 corpuscles, as six or seven to a small square is about the normal average when we are using a dilution of 1:200 such as has been described (twelve to fourteen cells per square in a dilution of 1:100).

Among the difficulties encountered in counting is the presence of a few corpuscles on or touching one or more of the lines *bounding* the space to be counted. Shall we count these out or in?

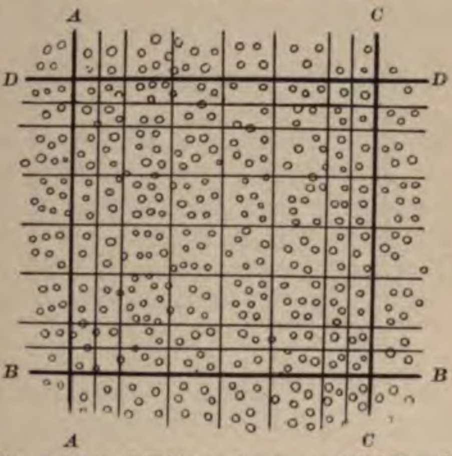

FIG. 6.—Field of Thirty-six Squares on Ruled Disc of Thoma-Zeiss Counter Covered with Normal Blood Diluted Two Hundred Times.

In counting, for instance, a field like that in Fig. 6, what are we to do with the cells which sit astride the lines AA, BB, etc.?

To get round this difficulty, it is best to make it a rule to count *in* all the corpuscles on or touching some two of the boundary lines (*e.g.*, AA and BB) and to take no notice of any cell on or touching the lines CC and DD. In this way the exclusions just balance the inclusions. Of course *all* cells *within* these outer boundary lines are to be counted whatever their position.

Beyond this the details must be settled by each man for himself. My own habit is to count through the squares in the order indicated by the track of the serpentine arrow in the accompanying Fig. 7, and to count by twos or threes.

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[1] Use only water—alcohol dissolves the cement which holds the ruled disc in place.

[2] See Reinert's "Zählung der Blutkörperchen," Leipzig, 1891, p. 48 *et seq.*

A movable stage makes the counting easier, especially for beginners. Either natural or artificial light may be used, with a small aperture diaphragm, and if the instruments are clean and the diluting solution fresh and free from sediment,[1] there is no difficulty in deciding how many cells each square contains, and no extraneous fragments to be excluded. We must distinguish the white corpuscles from the red, not by their size but by their stain if Toisson's solution is used, otherwise by their peculiar shining look when the lens is drawn up so as to put the red cells slightly out of focus. The blood plates are not noticeable and lead to no errors.

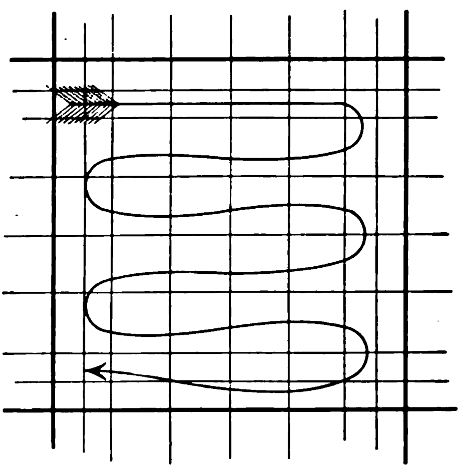

FIG. 7.—The Arrow Indicates the Order in which the Squares are Counted.

When the number of corpuscles in 360 squares has been counted the number is divided by 360 and multiplied by 800,000 (*i.e.*, by 200 to make up for dilution and then by 4,000, because each square is equivalent to $\frac{1}{4000}$ of a cubic millimetre), which gives us the number of corpuscles per cubic millimetre.

These figures need not be committed to memory, for we have marked on the instruments used all the data necessary for the calculation, *i.e.*, the dilution figures on the pipette and the area and depth of a single square on the counting slide.

(*e*) The importance of *cleaning the pipette* as soon as the counting is done is so great that it should be reckoned as one of the regular steps on every count. First water, then alcohol, and lastly ether must be sucked into the pipette and brought into contact with every part of the bulb and tube. After this air must be sucked or pumped through the tube until it is perfectly dry and the glass ball will roll about freely in the bulb without sticking anywhere.

These precautions take but two or three minutes, and if they are omitted and the blood dries in the pipette, it may take several hours' work to get it clean. Further, if it is not thoroughly *dried* after cleaning, the mixing of the blood when it is used next cannot be done accurately.

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[1] Most diluting solutions precipitate or accumulate spores, and need to be frequently renewed or filtered.

The first three steps of the above process (*i.e.*, the obtaining, diluting, and mixing of the blood) must be done as swiftly as is compatible with accuracy, but when once the blood is mixed in the pipette it can be kept there indefinitely and counted at leisure. None of the corpuscles are destroyed or lost, and if the bulb is thoroughly rolled and shaken up whenever we are ready to count the blood, no error results from keeping it twenty-four hours or more in the pipette.

It is not necessary, therefore, to carry a microscope to the patient's house or bedside; the pipette and the diluting solution are all that we need to take with us, and when the blood is mixed in the pipette, the latter's ends can be closed with a rubber band, and the blood carried home and counted at leisure. The pipette should be kept approximately horizontal during the transit.

COUNTING THE WHITE CORPUSCLES.

To make a reasonably accurate count of white corpuscles, using the "red counter" and the dilution of 1:100 or 1:200, we need to count an immense number of squares, far more than was necessary in estimating the red cells—in fact, at least ten times the whole ruled space. It is therefore far quicker and more accurate to use the "white counter" or large-bore pipette with a diluting solution which renders the red cells invisible and leaves only the white to be counted. Such a solution is the one-half of one-per-cent solution of glacial acetic acid in water. With this the white corpuscles stand out very clearly and the red can barely be seen at all. The technique is the same as that already described, with the following exceptions:

1. The drop of blood needed is nearly three times as large as that used in the "red counter"; it is about as big as can be made to stay on the ear without rolling off, even if we draw blood only to the mark 0.5. If we draw blood to the mark 1, as advised by Türck, we must make a deeper puncture and suck in the blood as it flows without waiting for the formation of drops.

2. The bore of the tube being large, it fills and empties more

readily. Hence our suction must be gentler, and it is rather harder to stop exactly at the mark 11. For the same reason the diluted blood will run out of the pipette if the latter is not kept nearly horizontal, and the bottle of diluting solution should accordingly be tipped up as we plunge in the point of the pipette, so that the latter is depressed as little and for as short a time as possible before suction begins.

3. Zappert's modification of the Thoma-Zeiss counting chamber should be used. Zappert's counting chamber (now supplied by Zeiss at the same price as the ordinary one, *i.e.*, 15 marks) differs from that ordinarily used in that the central square millimetre is surrounded by eight undivided squares of the same size (see Fig. 10). With this ruling one counts first the number of leucocytes in the central square (about 35 in normal blood) and then in each of the surrounding undivided squares. This gives us a total of about 300 leucocytes (in normal blood) as a basis for our calculations. The total so obtained is divided by 9, and then multiplied by 200 (provided we have diluted 1:20).

The advantages of the large-bore pipette are obvious. The only drawback is its expanse. The technique is not at all difficult.

Counting Both Red and White Cells with the Same Pipette.

We may avoid buying both large-bore and small-bore pipettes in one of the following ways:

1. We can count both red and white corpuscles with the "red counter."

2. We can count both red and white corpuscles with the "white counter."

The reason why we cannot use the "red counter" for counting white cells, unless modified in some way, is that in the whole ruled surface of the counting chamber not more than three or four white corpuscles are to be found in normal blood when diluted two hundred times. If we dilute less, we cannot see the cells distinctly, because they are so crowded. If we find, say, three white corpuscles as the number to be used as a basis in calculating the number of white cells in a cubic millimetre, the chance of error is very great, the multiplier being so large (2,000) and the multiplicand so small (3).

To get over this difficulty we may utilize the cells spread over the disc of the counting chamber *outside the ruled space* in one of the following ways:

(*a*) *By measuring the field of the objective used.* The writer's objective, No. 5 of Leitz, has a field of very nearly one-quarter of a square millimetre or one-quarter of the whole ruled space. Four fields of this lens, taken anywhere outside the ruled space, therefore, contain the same number of cells as will cover the whole four hundred small ruled squares.

(*b*) Another method is as follows: Cut out of black cardboard a square hole (see Fig. 8) of such a size that it will fit into the tube of the eyepiece—the square aperture allowing a space of just one-quarter of a millimetre (one hundred of the ruled squares) to be seen through it with a given objective (say Leitz No. 5). Four fields as seen through such an aperture can then be counted in various parts of the slide outside the ruled space as explained above.

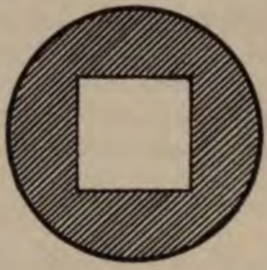

FIG. 8.

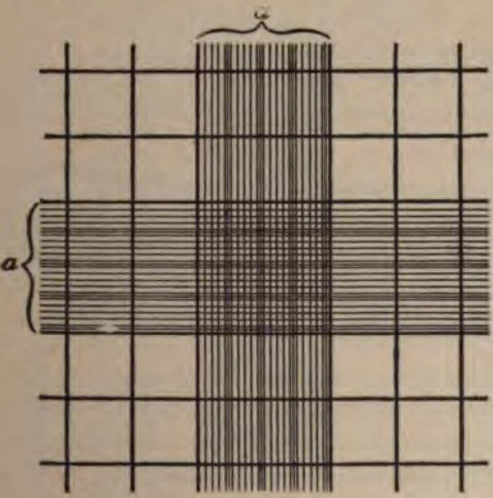

FIG. 9.—Zappert's Counting Chamber.

(*c*) For any one living where microscopic ruling on glass can be done at a moderate cost, by far the best way is to have the rest of the disc A (Fig. 5) ruled off as shown in Fig. 9. Leitz and Zeiss now supply instruments so ruled. I have not been able to hear of any one in America who could do such work at a moderate expense.

Whatever method of counting white corpuscles is adopted, we ought to have at least one hundred corpuscles actually counted to use as the multiplicand of our computation. A single drop from the white counter with a dilution of 1:10 gives us normally about seventy white corpuscles in the four hundred ruled spaces, and by repeating the process with a second drop the result may be made reasonably accurate. This was the method adopted by Rieder[1] in the immense number of counts made by him.

II. Durham's Modified Hæmocytometer.

In the Edinburgh *Medical Journal* for October, 1897, Herbert E. Durham, of Cambridge, England, describes a self-filling capillary pipette which has considerable advantages over the ordinary Thoma-Zeiss instrument. The account of the device is here given in his own words.

"As in the Gowers' instrument, there is a separate capillary pipette for measuring the blood, one for measuring the diluting fluid, a mixing vessel, and the counting chamber. A few words may be said about each of these.

"*Capillary Pipette.*—There is an obvious advantage in the use of a self-measuring pipette. It cannot go wrong by accident. Durham uses small pieces of thick-walled capillary tube—5 and 10 c.mm. in capacity. Such a pipette can readily be cleared by passing a piece of darning cotton by means of a needle through the bore of the pipette. It is best to wet the end of the cotton with ether.

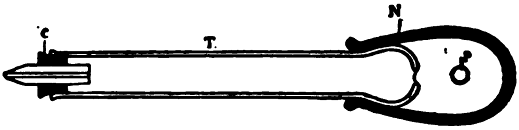

FIG. 10.—Cross-section of Durham's Automatic Blood-Pipette. *T*, Glass tube (like that of medicine-dropper); *N*, rubber nipple (like that of medicine-dropper); *p*, perforation in the nipple; *c*, cork holder, perforated by capillary pipette.

"Any one who has worked much with the Thoma-Zeiss pipette will know how troublesome it is to clean, especially when a number of observations have to be made in a limited time. The tiny pipette is mounted by means of a small cork (*c*) in a large glass tube (*T*), which is provided with a rubber nipple (*N*), having a lateral perforation (*p*) (Fig. 10)

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[1] "Beiträge zur Kenntniss der Leucocytosis," Leipzig, 1892 (Vogel).

"The *mixing vessel* consists of a small test tube ($2\frac{3}{8} \times \frac{7}{16}$ in. for 1 c.c., or $2\frac{3}{8} \times \frac{3}{8}$ in. for 0.5 c.c.). Several such tubes may be kept, so that a number of observations can be made if necessary. For thoroughly mixing the blood and diluting fluid, one or more small glass globules are placed in the tube. By using different colored glass globules, different specimens can be readily differentiated.

"For *measuring* the diluting fluid, *pipettes* containing 1 and 0.5 c.c. are used; these are remarked at 995 and 990 c.mm. and 495 and 490 c.mm. respectively. With these graduations the following dilutions may be obtained: 1:200, 1:100, and 1:50, with the appropriate capillary pipette.

"Having measured the diluting fluid, according to the eventual dilution desired, the blood capillary is filled by touching the exuding drop of blood and allowing it to completely fill itself.

"The hole in the nipple allows free air-way so that there is no hindrance to the action of capillarity. When filled, any blood on the outside of the pipette is rapidly wiped off, and the tube is inserted into the mixer until the point is one-half to three-fourths of an inch above the level of the contained liquid.

"The nipple is then held in such a way that the hole lies under the thumb of the operator. When this is the case it is slightly squeezed, and then, while the pressure is continued, the bulb is rotated so that the hole is free again. In this way the blood is squirted out, but not sucked back again. In order to wash out the remains of the blood the point of the capillary is dropped into the diluting fluid; the bore instantly fills itself. It is then withdrawn and the pressure and rotation of the nipple are repeated. This has to be repeated several times, and occupies a few seconds of time.

"To mix the blood and diluting fluid thoroughly, the mixer is placed between the opposed hands, which are rubbed backward and forward; the mixer is rotated thereby, and the glass globules cause a thorough dispersion of the corpuscles in the fluid.

"A drop of sufficient size is then placed upon the counting chamber, and the cover slip is slipped on sideways in the usual way. I prefer the Thoma-Zeiss counting chamber.

"The advantages of this method are:

"1. The ease and thoroughness with which the pipette can be cleaned.

"2. The manifest advantage of the self-measurement of the blood.

"3. The avoidance of the objectionable necessity of using the mouth to suck fluids into the pipette.

"4. The measurement of the diluent can be done carefully and calmly beforehand, and any error corrected without taking any more blood.

"5. The greatly smaller cost of the pipette.

"6. The same pipette is useful for making various dilutions in serum diagnosis, by using several mixing vessels filled beforehand with dilute fluid."

CHAPTER III.

OLIVER'S HÆMOCYTOMETER—CENTRIFUGALIZING THE BLOOD —HÆMOGLOBIN ESTIMATION—SPECIFIC GRAVITY— STAINED SPECIMENS—THE IODINE REACTION —BACTERIOLOGICAL EXAMINATION.

OLIVER'S HÆMOCYTOMETER.

RECENTLY a method of estimating corpuscles by means of their optical effect, and without directly counting them, has been introduced by Dr. Oliver. For practical purposes an actual counting of the corpuscles must be considered a necessity; not only since the number of leucocytes is not without importance (*e.g.*, in the diagnosis of enteric fever), but also since these cells may be so abundant that they may interfere with the use of optical methods, as in the case of leukæmia. Nevertheless the instrument is very accurate and useful in many cases. Its principle is based on the fact that if a small quantity of blood is gradually diluted with Hayem's solution[1] in a test tube whose sides are flattened so that its mouth forms a rectangle about 15 mm. by 5 mm., and a candle flame is looked at through the mixture, there is to be seen, *when a certain degree of dilution is reached*, a bright *horizontal* line on the glass. This line is made up of a large number of minute images of the flame, produced by the longitudinal striation of the glass. If the quantity and quality of blood used are in every instance the same, the degree of opacity depends wholly on the amount of Hayem's solution added. It is found that with normal blood the amount of diluting solution necessary to allow the image of the candle flame to be seen through the mixture is always the same, and can be very accurately fixed, so that a variation of one per cent in the number of corpuscles can be distinguished by noting the amount of diluting

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[1]		
Hydrargyri perchloridi	0.5	gm.
Sodii chloridi	1.0	"
Sodii sulphatis	5.0	"
Aquæ destillatæ	200.0	c.c.

solution which must be added before the image of the flame appears. To collect the blood, Oliver uses a capillary pipette con-

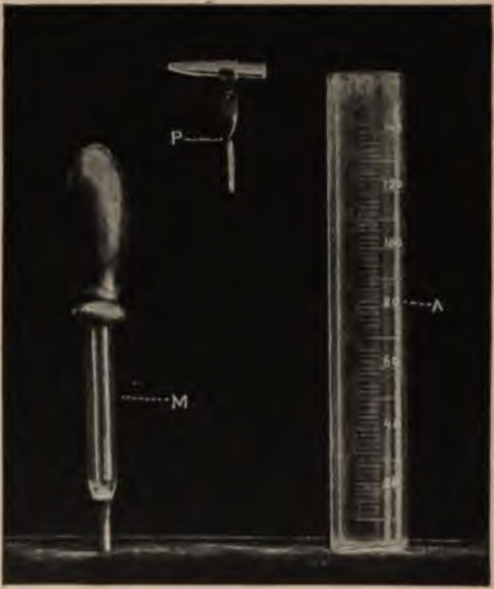

FIG. 11.—Oliver's Hæmocytometer. *A*, Graduated mixing tube; *P*, capillary pipette; *M*, dropper, with rubber nozzle fitting the capillary pipette.

taining about 10 c.mm. (one large drop), and used exactly in the same way as the v. Fleischl capillary pipette (see Fig. 11).

One pipette full of normal blood is gradually diluted in the flattened tube with Hayem's solution until a bright horizontal line caused by the image of candle flame becomes visible through the mixture. The point to which the column of the mixture *then* reaches is marked 100, and the space between that point and the bottom of the tube is divided into 100 equal parts. The point marked 100 is then equivalent to 5,000,000 red corpuscles; 90 = 4,500,000, 80 = 4,000,000, and so on, each degree on the scale corresponding to a difference of 50,000 corpuscles (Fig. 11).

Use of Oliver's Hæmocytometer.

The capillary pipette is first thoroughly cleaned and dried by passing through it a needle and thread saturated with water and then with alcohol and ether. It is then filled in the usual way, and the outside carefully and quickly wiped if necessary. The medicine dropper (previously filled with Hayem solution) is then connected with the polished blunt end of the pipette by means of the rubber tube (Fig. 11), and blood washed into the test tube. Speed is essential, else coagulation occurs. If the previous hæmoglobin estimation has shown ninety to one hundred per cent of coloring matter, we can safely add the diluting solution rapidly until the point marked 80 is reached. If the coloring matter is lower we must cease our rapid dilution correspondingly sooner. When we get near the point at which the flame image is likely to appear, the diluting fluid must be added a few drops at a time. After each addition put the thumb over the mouth of the tube and turn it upside down once or twice to mix the blood thoroughly, wiping the thumb each time on the edge of the tube so as to put back what fluid has adhered to it. At a certain point the image will suddenly become visible. It is seen soonest if we rotate the tube on its long axis, as the image becomes visible earliest at the sides of the tube, but dilution should be continued drop by drop until the horizontal line of light is just visible across the short diameter of the tube. The appearance of the incomplete line at the sides is a constant forerunner of the complete transverse line, and should put one on one's guard, as very close watching is needed to recognize it without overstepping the necessary dilution. The opacity remains uniform for many minutes. The whole process should be carried on in a perfectly dark room, and the dif-

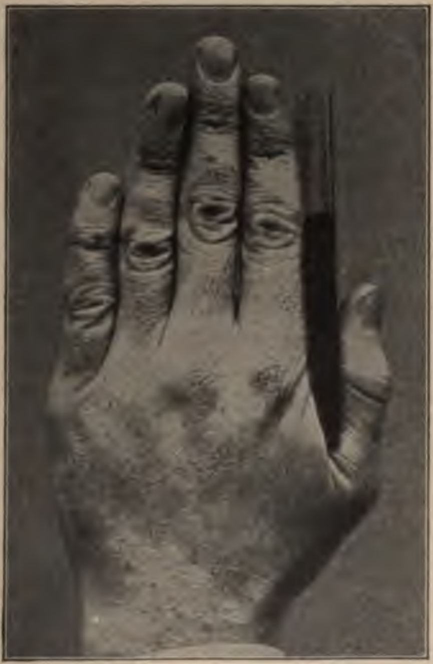

FIG. 12.—Showing the Method of Holding Oliver's Hæmocytometer.

fused light of the candle must be shut off from the eye. This is best done by fitting the tube into the hand, as shown in Fig. 12, with the long axis in line with the candle, holding the tube *close to the eye*, and standing about ten feet from the candle. In the use of both of his instruments Oliver employs only the small wax candles known as Christmas candles, whose flame is of the most convenient size.

After some experience with this instrument I find it simple, eye-saving, rapid, and sufficiently accurate in cases not associated with marked anæmia, as indicated by the previous hæmoglobin test. Its drawbacks are the impossibility of making any estimate of the white corpuscles with it and its gross inaccuracy in cases of severe anæmia (see Emerson, *Johns Hopkins Bull.*, January, 1903, and Baumgarten, *Johns Hopkins Bull.*, July, 1902).

THE HÆMATOCRIT.

The hæmatocrit of Hedin has undergone considerable modification and improvement and as remodelled and improved by Judson Daland has been used to some extent in this country. Its direct and obvious object is simply to ascertain the relative volume or mass of the corpuscles and of the plasma in a drop of blood; but the hope of its advocates has usually been that it would supplant entirely or mostly the long, tedious, and eye-destroying process of counting with the Thoma-Zeiss instrument.

To use the Daland hæmatocrit we prick the ear as usual and with the help of a bit of rubber tube attached to one end of the capillary tube (Fig. 13) suck in enough blood to fill it entirely.

As soon as it is full, put the finger (greased with vaseline) tightly over the free end of the glass tube and then, *but not till then*, draw off the rubber tube and adjust the glass as quickly as possible in the place prepared for it on one of the horizontal arms of the whirling machine (Fig. 13). A similar tube (empty) should be put on the other arm of the crosspiece to make the balance true. The handle of the instrument is then revolved at least seventy times a minute for two minutes, at the end of which time (sometimes less) the column of blood cells is packed so tight that no further whirling has any effect on its length.

To estimate the number of red corpuscles from the length of the column, we call each degree of the scale on the tube 100,000 cells, or a little more. Thus if the blood column in the tube ends at about the mark 50, we consider that the blood has rather more than 5,000,000 red corpuscles per cubic millimetre. So far all observers agree on the figures, but as to just how much more or less than 100,000 each degree on the scale is worth there is some variation between different observers. Daland[1] finds that the degree of the scale on the capillary tube corresponds to 99,390 corpuscles.

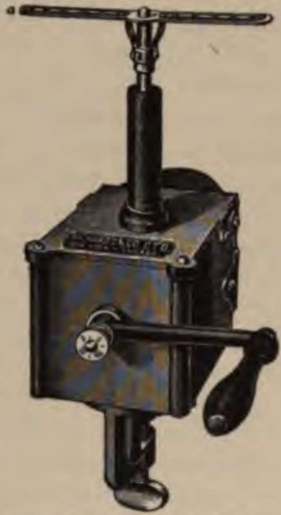

FIG. 13.—Daland's Hæmatocrit. Two capillary tubes in place on the horizontal whirling beam. The instrument is to be fastened to the edge of some solid and bulky piece of furniture by means of the thumb screw seen at the bottom of the cut. If not very tightly secured, it will work loose when the handle is revolved rapidly.

So far as I can learn, the use of this instrument in Europe has been chiefly for the direct information it affords as to the *volume* of the red cells and the amount of respiratory surface in the blood, rather than for the indirect information it may give us as to the *number* of the red cells. It does not seem as yet to be supplanting the Thoma-Zeiss counter.

Its bulk and the noise it makes must for the present, I think, prevent its extensive use outside of hospitals. The noise it makes is a very loud and disagreeable one, and will deter many from using it in private practice.

Emil Aspelin ("Rüneberg's Festschrift," 1903) has recently made a number of experiments with a modified instrument, using a longer tube and a mixing bulb like that in the Thoma-Zeiss instrument. Here he mixes the blood with a diluting solution, and after thorough centrifugalization is able to estimate with reasonable correctness the number of leucocytes as well as of red cells. Still the time consumed is greater than that necessary to make a count of white cells with the Thoma-Zeiss instrument, and for the red cells the new instrument, even in Aspelin's hands, is often far from accurate.

Emerson (*Johns Hopkins Bull.*, January, 1903) finds the hæmatocrit "useful in determining the presence of lipæmia, cholæmia, hæmoglobinæmia, etc., but not to count the cells."

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[1] University Med. Mag., November, 1891.

HÆMOGLOBIN ESTIMATION.

1. Tallqvist's Hæmoglobinometer.
2. Dare's "
3. Oliver's "
4. v. Fleischl's "

Until recently the instrument most used both here and in Europe was that of v. Fleischl. In France Hayem rules supreme in the matter of instruments, as in everything else concerning the blood, and in England Oliver's apparatus is used to a certain extent. Very recently, however, a contrivance originated by Tallqvist[1] has come into use and deserves, in my judgment, to supplant all others in clinical work. I shall therefore describe it first.

1. Tallqvist's Hæmoglobinometer.

A drop of undiluted blood is soaked into a bit of filter paper of standard quality and compared (by ordinary reflected daylight) with a paper color scale of ten tints, ranging from ten per cent to one hundred per cent. The scale was prepared by imitating in water color the tint of the blood of anæmic patients (using the v. Fleischl instrument) when soaked into the standard filter paper. The water-color standard colors were then reproduced in lithograph, and the lithographed scale bound up with fifty sheets of the standard filter paper makes an apparatus which can be easily slipped into the pocket and carried to the bedside.

In making the comparison the blood stain is put against[2] a background of white filter paper beside the color scale, and moved along until a match is found. The comparison should be made as soon as the stain has lost its humid gloss and before it is thoroughly dry. Artificial light cannot be used. Errors of ten per cent are possible, but it is my belief that far greater errors than this are frequently made with v. Fleischl's or Oliver's instrument in the hands of the great majority of physicians. Tallqvist's scale costs but $1.25, and can be used by any one with sufficient accuracy for practical purposes, and with a celerity that makes hæmoglobin estimation no more of an undertaking than feeling the pulse. I have used the instrument in several hundred cases, and have never yet been misled by it, nor found a greater error than ten per cent in comparison with Oliver's or Dare's instrument.

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[1] Tallqvist, St. Paul Med. Jour., May, 1900.

[2] Never blot it.

II. Dare's[1] *Hæmoglobinometer.*

This excellent instrument is undoubtedly more accurate than Tallqvist's, and would be preferable to all others but for its cost ($20), its bulk, and the time necessary to make an observation and to clean the parts.

As in Tallqvist's method, undiluted blood is used, and this constitutes an advantage over both v. Fleischl's and Oliver's instruments. The blood is drawn by capillary attraction into the slit between two slabs of glass, one transparent, the other translucent and white, so as to diffuse the light used for illumination.

The color of the blood is then compared with different portions of a circular disc of colored glass revolved by means of a thumb screw so that different tints are successively brought side by side with the blood tint. Transmitted light from a candle is used for illumination, and the observation is made through a tube, which effectually excludes all extraneous light. As we turn the screw and bring different tints of the glass standard into comparison with the layer of undiluted blood, the percentage of hæmoglobin can be read off from the etched scale which appears at a point opposite the color aperture. The sharply bevelled edge of the opening rests directly over the reading indicated. A pivoted black screen protects the observer's eyes from the direct light of the candle, and may occasionally be brought over the color apertures so as to rest the eye.

The instrument is so made that blood film and standard color disc are viewed side by side in a horizontal plane through two circular holes 5 mm. in diameter which are considerably magnified by a lens in the telescoping camera tube.

In using the instrument we need no dark room—a great advantage. The instrument is simply pointed at some dark surface—a dark coat or corner. In order that the blood and the color disc should be equally lighted, it is essential to see that any curve that exists in the candle wick should point straight toward or away from the centre of the instrument in line with the juncture of the springs which support the candle.

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[1] Phila. Med. Jour., October, 1900.

The reading should be completed before the blood film begins to shrink in from the edges, *i.e.*, within ten minutes.

The advantages of Dare's instrument are:

1. Its accuracy; using undiluted blood and making allowance as it does for the color curve, it is, I believe, more accurate than any other clinically available instrument.

2. Leucocytosis does not disturb the reading (as it does in v. Fleischl's instrument).

3. The errors and waste of time incident upon dilution are avoided, since the instrument uses undiluted blood.

4. No dark room is needed.

5. It can be used and cleansed much more quickly than any other instrument except Tallqvist's.

My reason for preferring Tallqvist's instrument despite these merits of Dare's are:

1. Because accuracy greater than that obtainable with Tallqvist's instrument is seldom practically important.

2. Because an observation can be made with Tallqvist's hæmoglobinometer in about one one-tenth of the time needed for using any other instrument, *i.e.*, in about twenty-five seconds.

3. Because the Tallqvist instrument takes so little room and needs no cleaning or preparing for use.

4. Because it is so cheap.

III Oliver's Hæmoglobinometer.

Oliver's instrument corrects two errors which are inherent in v. Fleischl's

1. It has no sliding scale of color, but compares the blood tint successively with definite tints of glass, each of which is even. The tints are worked out to correspond to the specific dilution curve of blood, for:

2. Since every colored liquid changes color at a different rate when diluted, the dilution curve of *blood* does not correspond to that of *glass* (which behaves in this respect like a liquid). The glass wedge of v. Fleischl's instrument represents a single color regularly diluted and does not correspond in its degrees to the colors of blood diluted at a similar rate. The scale of Dr. Oliver's instrument is measured to correspond to the actual colors of the blood's dilution curve by means of the tintometer.

In other respects the principle of the instrument is like v.

Fleischl's, and the method of using the two is practically the same except that in Oliver's reflected light is used instead of transmitted light. Oliver's instrument consists of a series of twelve tinted glass discs corresponding to the hæmoglobin percentages from 10 to 120 and arranged in two rows (see Fig. 14, *a*). The intermediate degrees are measured by means of "riders" of colored glass, which can be laid on top of the primary color discs so as to deepen the tint seen

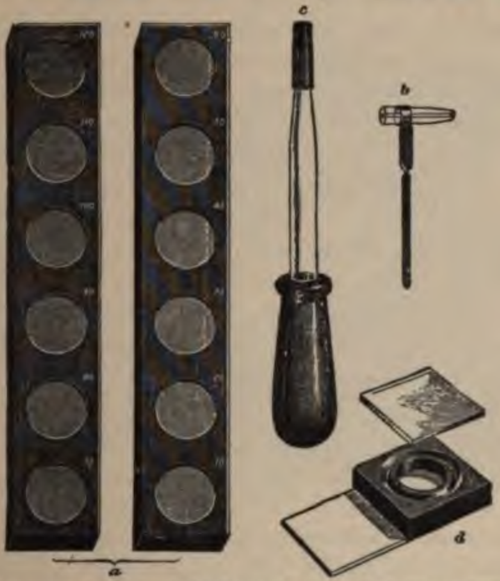

FIG. 14.—Oliver's Hæmoglobinometer. *a*, Standard color discs; *b*, capillary pipette; *c*, washing tube; *d*, mixing cell.

The capillary pipette (Fig. 14, *b*) is somewhat stouter than v. Fleischl's, but is used in the same way to collect the blood, which is then forced out of it with water from a medicine dropper (which is fitted with a rubber tube to slip over the blunt end of the pipette) (Fig. 14, *c*) and washed into a mixing cell (Fig. 14, *d*) similar to v. Fleischl's, except for the absence of a central partition. Here the blood is mixed in the usual way with water and the cell filled to the brim and covered with a small glass plate; a bubble always forms, but by turning the cell or moving the cover-glass we can usually get the troublesome shadow thrown by the bubble out of the color field. The blood thus prepared is brought close to the scale and there compared with the tint of the different standard color discs. If it matches one of them the observation is complete; if not we use one of the glass riders, which enables us to read within two and a half degrees A fuller set of riders can be obtained so as to make it possible to read down to one per cent.

The standard is usually arranged for candle light, but another set of discs can be obtained adjusted to daylight readings. The latter are less accurate. The same precautions as to the exclusion of outer light by means of a "hydroscope" tube, resting the eye frequently, etc., must be observed with this instrument as with v. Fleischl's. [It can be obtained of J. H. Smith & Cie., Zurich (Wollishoften), for 115 francs plus duties and expressage, or of the Tintometer Company, 6 Farringdon Avenue, London, E. C.] The candle should be placed three or four inches from the instrument and arranged to light both the blood and the color discs alike.

A word as to the use of the riders. The instrument as used for clinical work usually has two riders: the one having the deeper tint is used on the upper half of the scale, the other on the lower. Suppose we have decided that the blood color is between 60 and 70. Put the rider on the 60 disc and compare again. If the blood is darker than the 60 disc plus the rider, the percentage is approximately 67½ (since it is higher than 60 + 5 [the rider] and lower than 70. If it just matches the 60 plus its rider, the reading is 65. If the blood is paler than this, yet darker than 60, it is about 62½. An error of about two degrees is obviously inevitable.

IV. Use of v. Fleischl's Hæmometer.

(*a*) Fill on one side of the metallic cell (*a*, Fig. 16) about one-quarter full of distilled water. Put the end of the little pipette (*B*) horizontally into the side of the blood drop, which will at once fill the tube by capillary attraction. Quickly wipe away any blood that may be on the outside of the pipette. Then put it into the water contained in one of the partitions of the metallic cell and rattle it quickly back and forth, so that the water may be forced in first at one end and then at the other.

(*b*) After this the expulsion of the blood may be completed by forcing water from a medicine dropper through the capillary pipette and into the compartment where the mixing has been begun. Using the metal handle of the pipette, mix the blood and water in every part of the compartment. Then fill both compartments of the cell to the brim with distilled water, and adjust the compartment containing the clear water so that it comes over the slip of colored glass, while through the compartment containing the blood light thrown upward by the reflector below passes directly to the eye. Turn the thumb screw (see Fig. 16, *T*) back and forth until the color of the glass is the same as that of the blood, and read off the number on the scale which corresponds to that color. This gives the percentage of hæmoglobin, 100 being the color of normal blood for men and 80–90 for women.

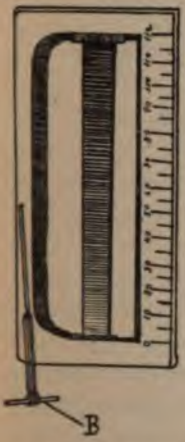

FIG. 15.—*A*, Colored glass; *B*, capillary pipette.

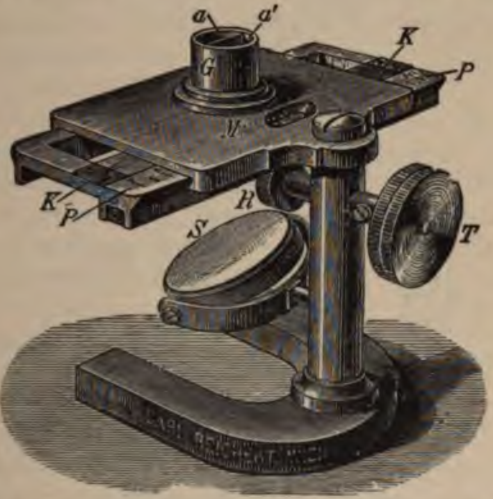

FIG. 16.—v. Fleischl's Hæmometer. *a*, Partition into which blood is put; *a'*, partition into which water is put; *G*, mixing cell; *K*, *K*, colored glass slip (see Fig. 15, *A*); *P*, *P*, metal frame on which scale is marked; *R*, *S*, reflector; *T*, screw which moves the frame, *P*, *P*.

(*c*) *Matching the colors* may be somewhat aided by observing the following precautions:

1. *Do not stand* (*or sit*) *facing the light, but sideways.*

2. *Use as little light as possible.*

3. *Roll up a piece of paper* (*preferably black*) *into a tube* of such size that it will fit over the metallic cell (*D*, Fig. 17), and rest on the platform of the instrument.

4. *Use first one eye and then the other, and never look more than a few seconds at a time.*

5. *Move the thumb screw with short, quick turns rather than*

slowly and gradually, for sudden color changes affect the retina more than gradual ones.

6. If the preliminary reading shows one of thirty per cent or less, two or three pipettes full of blood should be used and the reading divided by 2 or 3. A considerable error can thus be avoided.

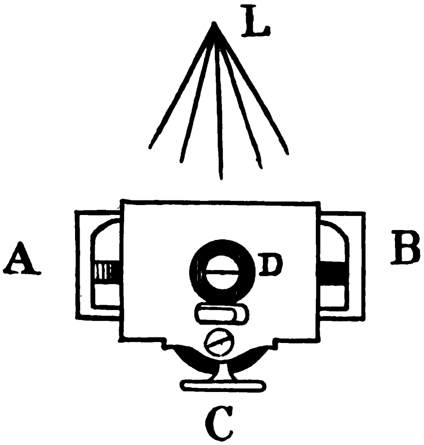

FIG. 17.—*L*, Light; *A* and *B*, right positions for observer; *C*, wrong position for observer; *D*, cell in place.

Necessary Errors.

A considerable error is absolutely necessary, inasmuch as the bit of colored glass to be seen at any one time through the aperture of the instrument is not (like the blood) all of one tint, but includes a *variation of twenty per cent in color, i.e.,* if the glass appearing at one end of the aperture is opposite 50 on the scale, that seen at the other end of the aperture will either be at 30 or at 70.

To avoid these and other difficulties with v. Fleischl's instrument various modifications of it have been proposed, the best of which is Miescher's.

In using Miescher's modification of v. Fleischl's instrument the dilution is carried on in a capillary pipette like that of the Thoma-Zeiss instrument, distilled water being the diluent. From the mixing bulb of the pipette the diluted blood is blown into *one* compartment of each of the two cells (one 15 mm. deep, the other 12 mm. deep) which are supplied with the instrument. The other compartment in each cell is filled with water. The grooved cover-glass is slid along the projecting partition of each cell, and each cell then covered with a diaphragm which transmits a ray of light corresponding to not more than three degrees of the scale, "thus giving practically a single color of the glass wedge for comparison with the blood" (Emerson). Candle light is used.

The reading of the smaller cell should be four-fifths that of the larger, and one reading may be used to control the other. The table supplied with the instrument translates the data obtained into hæmoglobin percentages or grammes per 100 c.c. of blood.

The instrument is very accurate, but no better than Dare's, which costs less than half as much.

As recently pointed out by Emerson (*loc. cit.*), the readings of most hæmoglobin scales (100 per cent being made to correspond to about 13.8 gm. of hæmoglobin per 100 c.c. of blood) cannot be applied directly to *children's* blood.

The child under five years has normally but 10 to 16 gm. per 100 c.c., which would correspond not to 100 per cent, but to 75 to 80 per cent. Similarly the normal for a child from five to fifteen years is 80 per cent; from fifteen to twenty-five years, 88 per cent. It would be better, as Emerson says, to express our readings in grammes per 100 c.c. rather than in per cent.

ESTIMATING THE SPECIFIC GRAVITY OF THE BLOOD.

The simplest and most available method for clinical use is that of Hammerschlag,[1] a modification of Roy's[2] method. Chloroform is heavier than blood; benzol is lighter. Mix in a urinometer glass such quantities of the two that the specific gravity taken by an ordinary urinometer is about 1059, *i.e.*, that of normal blood. Puncture the ear, draw a drop of blood into the tube of a Thoma-Zeiss pipette, a small medicine dropper, or any other capillary tube, and blow it out again into the chloroform-benzol mixture. The blood *does not mix at all* with these liquids, but floats like a red bead. If it sinks to the bottom add chloroform, if it rises to the top add benzol, until finally the drop remains stationary in the body of the liquid, showing that its specific gravity is just that of the surrounding mixture. Then take the specific gravity of the liquid, as we do of urine, and you have the specific gravity of the drop that floated in it. The following precautions are needed:

1. Have the inside of the urinometer glass perfectly dry and clean; otherwise the drop of blood may cling to it and flatten out against it.

2. It is usually well to have more than one drop of blood in the glass in case any mishap occurs with the first one.

3. Add the chloroform and benzol a few drops at a time, and

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[1] Wien. klin. Wochenschrift, iii., 1018, 1890.

[2] Proceedings of Physiological Society, 1884.

after each addition stir the whole mixture thoroughly with a glass rod.

4. If we have reason to suppose the blood will be lighter than normal (*i.e.*, if the hæmoglobin is probably low, ***vide supra***), it saves time to start with a lighter mixture of chloroform and benzol.

5. Avoid having any *air* within the blood drop. This can generally be seen either in the capillary tube or after the drop is in the mixture. It is safer to take the *middle portion* of the blood drawn into the capillary tube, as both the first and the last portions of the column are more apt to have air in them.

6. The whole process should be done as quickly as possible, else the chloroform or benzol may evaporate or work into the blood drop and so affect its weight.

It is better to have a urinometer with a scale running as high as 1070, but this is not essential, for the clinically important specific gravities are *low*, not high.

The importance of the specific gravity of the blood, as hinted above, is not so much for itself, but because it runs parallel to the percentage of hæmoglobin and gives a figure from which the latter can be computed.

The specific gravity of the blood varies very little (except in *dropsy* from any cause), and in the corpuscles themselves the variable element is the hæmoglobin.[1] Consequently in most non-dropsical patients the specific gravity of the whole blood varies directly as the hæmoglobin. The following exceptions to this rule must be borne in mind.

1. In leukæmia the specific gravity is relatively higher than the hæmoglobin on account of the weight of the leucocytes.

2. In pernicious anæmia with high color index (see below) the hæmoglobin is about two per cent higher than we should gauge it to be judging by the specific gravity.

To estimate the percentage of hæmoglobin from the specific gravity, one of the following tables may be used, modified from Schmaltz, "Pathologie des Blutes," etc., Leipsic, 1896, using a direct weighing method. Apparently a degree of specific gravity means much more at the top of the scale (*i.e.*, 6.6 per cent) than at the bottom ($1\frac{2}{3}$ per cent). This table has been verified by the research of Yarrow (*University Med. Mag.*, 1899) through comparison with a standard solution of 13.77 gm. of prepared hæmoglobin in normal salt solution (up to 100 gm.). It appears to be very accurate.

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[1] Except in dropsy in which the corpuscles themselves may get water-soaked.

Spec. Grav.		Hæmoglobin.			Spec. Grav.		Hæmoglobin.		
1030	=	20	per cent.	±	1049	=	60	per cent.	±
1035	=	30	"	"	1051	=	65	"	"
1038	=	35	"	"	1052	=	70	"	"
1041	=	40	"	"	1053.5	=	75	"	"
1042.5	=	45	"	"	1056	=	80	"	"
1045.5	=	50	"	"	1057.5	=	90	"	"
1048	=	55	"	"	1059	=	100	"	"

STUDIES OF FINER STRUCTURES OF THE BLOOD.

The study of dried and stained specimens with the help of the aniline dyes gives us much of interest and importance in regard to the blood. More can be told about a given case by the study of a dried and stained cover-glass specimen than by any other single method.

Preparation of Cover-Glass Specimens.

(*a*) Covers carefully cleaned and polished are arranged at the bedside in such position that we can quickly pick them up without touching their surfaces (see Fig. 1).[1] The ear is punctured in the usual way, and one of the cover-glasses touched to the summit of the drop as soon as it emerges. This cover-glass is then let fall upon another in such a way that their corners do not coincide (Fig. 18). If the covers are clean, the drop spreads *at once* over their whole surface; as soon as it stops spreading, slide off the top one *without lifting them apart*, but exactly in the plane of their surfaces. Have a gas or alcohol flame at hand and dry instantly if you want to get the very best specimens; but this is not at all necessary for most clinical purposes. The *under* cover-glass is always better spread than the *upper*.

The above method needs a good deal of practice. (*b*) An easier way of preparing blood films is as follows:

Put a moderate sized drop of blood on a glass *slide* (not a cover-glass) near one end. Hold another slide (or a cover-glass) against the first in the position shown in Fig. 19. Move the slide along in the direction shown by the arrow so as to spread the blood drop over the whole length of the glass as thinly as possible. The quicker the whole process is performed the better will be the results. After drying the film in the air it can be fixed and stained as below described.

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[1] I often poise them on corks so that their corners are readily accessible to the fingers. The process of making blood films is far easier if another person prepares the drop for us so that we can stand ready with a cover-glass in each hand to catch the drop as soon as it emerges.

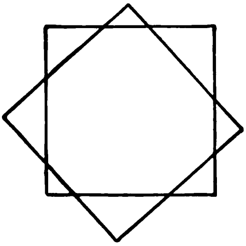

FIG. 18.

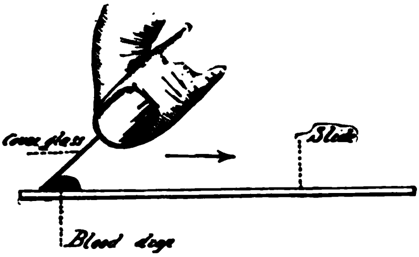

FIG. 19.—Spreading Blood on a Glass Slide.

Fixing the Films.

These films have now to be *fixed*, and this process is best combined with that of staining as is done by Wright's method (see below). If other staining methods are to be used, the films must first be fixed either by heat or by half an hour's immersion in absolute alcohol and ether (equal parts), or by the same mixture (30 c.c each) plus five drops of a saturated alcoholic solution of corrosive sublimate (five minutes' immersion), by chromic acid two per cent, or by exposure to the vapor of forty-five-per-cent formaldehyde. I have used all these methods, but found none of them to compare favorably with Wright's method.

The method of fixation by alcohol and ether needs little comment, the cover glasses being simply left in the mixture half an hour or as much longer as is convenient. Half an hour is enough. For Ehrlich triacid stain we use dry heat. The best way to do this is in a dry-heat sterilizer at a temperature of 115°–155° C., according to the size and construction of the oven and the kind of stain used. The temperature must be watched very closely, and as soon as it reaches the desired point the heat should be removed. It needs about five minutes to get the temperature to 150° C., and as soon as it gets there the specimens should be taken out. The thermometer bulb must rest as near as possible to the blood films without actually touching them.

STAINING.

I. Wright's Method.

Within the past year hæmatological technique has been notably simplified and improved by the introduction of a stain far superior in my opinion to any previously in use. I refer to Wright's modification of Leishman's stain, which in turn is a modification of Jenner's. Jenner introduced the use of methylic alcohol at once as a solvent for staining materials and as a means of fixing blood films upon glass. Leishman simplified and improved the method of using a stain which in itself differs but little from Jenner's. Wright showed us a much quicker and easier method of preparing the stain, the essential pigments in which are polychrome methylene-blue and Grübler's yellow eosin. For details of preparing the stain see Wright's article.[1] The stain must be kept in a *tightly-corked* bottle since evaporation soon makes it precipitate, and so spoils any preparation stained with it. I have noted no deterioration in bottles used during the last six months.

The process of staining is quicker and simpler than any other known to me, and even if it is not carried out precisely according to the directions given below, a fairly presentable specimen is almost always to be obtained.

TECHNIQUE.

1. Drop upon the blood film with a medicine dropper as much of the stain as it will hold without spilling off, and leave it there for one minute. This is chiefly to fix the film.
2. Add to the fluid on the cover-glass (or slide) sufficient water drop by drop to make visible a greenish metallic scum upon the surface. For a ⅞-inch square cover-glass six to eight drops are usually needed, but the exact amount does not make any essential difference. Let the stain thus diluted remain for about two minutes upon the film.
3. Wash the film in tap water and let it stand in water for one or two minutes more, or until the thinner portions of the film are yellowish pink. Water washes out part of the blue dye and differentiates the stain.

James H. Wright: Jour. Med. Research, January, 1902.

4. Dry cautiously with blotting paper or filter paper and mount in balsam.

The whole process should not consume more than five minutes' time. (The stain may be had at the Harvard Coöperative Society store, Boylston Street, Boston.)

This stain is the best known to me not only for leucocytes and erythrocytes, normal and abnormal, but also for malarial parasites, basophilic granulations of red cells, and all purposes for which one uses a blood stain at all

II. Ehrlich's Method.

Far inferior in most respects is Ehrlich's tricolor mixture, which is made as follows:

Saturated watery solution of orange G	6 c.c.
" " " " acid fuchsin	4 "

To these add a few drops at a time, shaking between each addition

Saturated watery solution of methyl green................. 6.6 c.c.

Then add:

Glycerin	5 c.c.
Absolute alcohol	10 "
Water	15 "

Shake well for one to two minutes. Let stand twenty-four hours. Do not filter. G. Grübler's colors are best.

The staining process is simple. A drop of the stain is simply spread over the surface of the cover-glass specimen with a glass rod and washed off again with water after five minutes, or as much longer as is convenient. If the specimen look too dark (brown or red instead of orange-yellow), it is not because of overstaining, but because of *underheating.*

If overheated, the specimen looks pale lemon yellow to the naked eye, and under the microscope everything is blurred and dim.

The Iodine Reaction.

Iodophilia, so called, is the reaction which the neutrophilic leucocytes show when brought in contact with a drop of the following solution:

Iodine	1 gm.
Potassium iodide	3 "
Water	100 c.c.
Gum arabic	50 gm.

A drop of this mixture is put on a slide and into it we press a film of blood without any previous fixation or preparation of any kind. Use an excess of the iodine mixture and then squeeze out the excess by gentle pressure on the cover-glass lest the dense color of the fluid obscure the field. When such a slide of normal blood is examined, the red cells are found to be uniformly colored a bright yellow upon a much fainter background, while the white corpuscles are stained of about the same tint, their nuclei being somewhat more refractile. This contrast between the nucleus and protoplasm is sufficiently distinct to permit one readily to differentiate the various forms of white cells. In certain pathological conditions, such as septicæmia or uræmia, the uniform yellow coloration is broken by the appearance in the protoplasm of the polymorphonuclear neutrophiles of reddish-brown granules, or a diffuse brownish coloration, and by the presence of small and large masses outside the corpuscles similarly colored. This condition is the "iodine reaction," and as suggested is of two distinct types, namely, (1) the extracellular, and (2) the intracellular.

1. *Extracellular Reaction.*—The masses seen outside the cells are round, oval, or slightly irregular, varying in size from 2 to 6, or even 8 μ in diameter, and of a copper-red color. They may be free, but are usually found in fragments of protoplasm which appear to be the débris of broken-down leucocytes.

2. *Intracellular Reaction* (see Figs. 20 and 21).—Within the cells the reaction occurs almost invariably in the neutrophiles. Here the appearance is extremely varied, the granules being of almost any depth of color from a light orange to the deepest brown, and of various sizes. They may be scattered evenly throughout the protoplasm, grouped about the neucleus, or, in rare cases, at the periphery of the cell. In sharp contrast to the round or oval extracellular bodies, those within the cells are for the most part irregular in shape. In many of the neutrophiles the reaction is shown not by a granular appearance of the protoplasm, but by a diffuse brownish discoloration, the depth of which varies within wide limits. In rare cases basophiles and myelocytes react, but here the picture is a different one, for instead of many granules scattered throughout the protoplasm one finds a more or less distinct single row of relatively large brownish areas about the nucleus We have never observed any brown color, either diffuse or granular, in the eosinophiles.

It is important to note that in some specimens only a few neutrophiles are found which are abnormal. The intensity of the color appears to be of as much importance as the number of corpuscles showing it. Not infrequently a large number of leucocytes are seen absolutely unaffected by the iodine solution before any are found with the characteristic coloration. With other cases scarcely any normal ones can be demonstrated. In our examinations we have, as a routine, counted at least one hundred cells; if in that number none are observed with either a diffuse or granular stain, we consider the reaction negative.

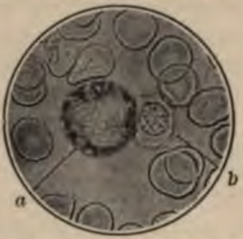

FIG. 20.—*a*, Strong Iodophilia in a Polynuclear Leucocyte; *b*, Normoblast.

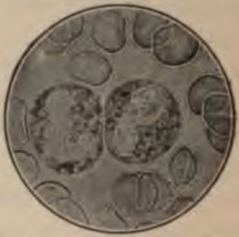

FIG. 21.—Moderate Iodophilic Reaction in Two Polynuclear Leucocytes.

Differential Counting.

The only procedure in the microscopic examination of stained specimens which needs any description is that of making the so-called "differential count" of the leucocytes (*i.e.*, determining what percentage of the leucocytes present belongs to each of the subvarieties as described on pages 60–67). To do this accurately we should examine at least five hundred leucocytes—the examination being simply the classification of them under their different subvarieties. A movable stage is very convenient though not essential for this purpose. With such a stage the technique is simply to start with the lens in, say, the *upper left-hand* corner of the blood film and, by turning the screw of the mechanical stage, move the preparation slowly past the eye until the *upper right-hand* corner is reached. During this process, as the cells appear in the field they are checked off and put down under one or another heading. Then move the stage so that the lens is just one field's diameter nearer the *right-hand lower* corner of the preparation, and go back again from right to left, following the serpentine track indicated above in Fig. 7. To move the lens just one field's diameter we have only to fix the eye on a cell at the extreme edge of the field, and then move the stage till that cell disappears out of sight on the *opposite* side of the field. Thus we avoid any chance of counting the same cells twice, and yet are sure not to miss seeing any.

As we go back and forth in this way, we notice chiefly the white cells, of course, but yet keep our eyes open for any unusual appearances in the red cells. Usually these move by in a monotonous stream, one looking much like another, but in pathological blood we must always be on the lookout for nucleated red cells, degenerative changes, and variations in size and shape. In malarial cases, of course, our scrutiny is directed chiefly upon *red* cells.

If we have not the help of a movable stage we try to do the same thing moving the slide with the fingers. With moderate care there is no danger of counting the same cells twice, but we cannot help missing a good many altogether, so that although accurate the process takes longer.

When leucocytosis is present, at least one thousand leucocytes can be found in a single well-spread seven-eighth-inch cover-glass specimen. In normal blood we may need to go through two or three covers.

BACTERIOLOGICAL EXAMINATION.

Blood obtained by the ordinary method of puncture is not fit for bacteriological examination.[1] The following is the better way:

Sterilize the skin over the flexor surface of the bend of the elbow, and wash off thoroughly the agents used for sterilization with boiled water or boiled normal salt solution. Have an assistant grasp the upper arm so as to prevent the venous return and distend the large veins at the elbow. Into the most prominent of these plunge a sterilized hollow needle connected with the bulb of a sterilized syringe. All traces of antiseptics must be carefully washed out of the needle and the syringe bulb before using.

When the needle penetrates the wall of the vein the blood usually begins to flow into the bulb of the syringe, and this is hastened by gently withdrawing the piston until 5 to 10 c.c. of blood are in the bulb. Then withdraw the needle, press a pad of sterilized gauze over the wound, and expel the blood before it coagulates into a flask of nutrient bouillon or melted agar-agar.

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[1] See Kühnau's comparative experiments in Deut. med. Woch., 1897, No. 25.

The further examination of cultures falls outside the scope of this book.

In the above procedure the only difficulties are: 1 Sometimes it is hard to find a vein and to get the needle into it. 2. Occasionally we get the needle entirely through the vessel into the tissues on the other side.

If the blood does not flow readily into the bulb one of these two mistakes is usually the cause, but occasionally in those whose vessels are very small or whose circulation is very feeble (as in the moribund) it is very hard to get the requisite amount of blood. Only practice helps us to avoid these difficulties.

The procedure causes hardly more pain than the use of an ordinary subcutaneous injection; the process of sterilization is usually more irksome to the patient than the puncture

Bleeding is trifling, and within twenty-four hours there is usually no trace of the puncture left. A sterilized dressing with moderate pressure should be applied

Estimation of the Time and of the Completeness of Coagulation.

In certain conditions, particularly in acute exanthemata, clotting is slow or fails to occur. This is still more marked in the various forms of the hemorrhagic diathesis. In obstruction in the biliary tract, with or without jaundice, clotting may be greatly delayed, and this fact is of great importance to the surgeon with reference to the question of operation.

Hayem has called attention to the fact that in purpura hæmorrhagica the blood clot may form, but fail completely to retract. He further believes that the blood of pernicious anæmia may be distinguished from specimens obtained in cases of secondary anæmia by the fact that in pernicious anæmia there is an incomplete formation of serum.

In both these conditions the blood plates are greatly diminished. Hayem has found similar changes in some other cachectic conditions.

The importance of these facts in the prognosis of purpura may be considerable—the severer forms being thus distinguishable from the milder types (according to Hayem) even during the remissions or non-hemorrhagic stages of the disease.

For the estimation of coagulation time the simple little instrument devised by Wright is sufficient. This consists simply of a set of from six to twelve capillary tubes of about the same calibre (0.01 to 0.0125 inch) into each of which a blood column about two inches long is aspirated. The tubes are then set perpendicularly in a rack and at regular intervals the condition of the blood is tested by blowing into one of the tubes. When coagulation occurs, the tubes are found to be blocked with clot.

Normally coagulation occurs in these tubes in about three minutes. In disease, especially in cases with biliary obstruction, coagulation may not occur until ten to fifteen minutes have elapsed.

OTHER METHODS OF BLOOD EXAMINATION.

It is perhaps worth while briefly to mention some other methods of blood examination of which no account will be given.

1. Determination of the *alkalinity* of the blood. No accurate and clinically available method has yet been devised. Despite the interesting work of Kraus, Caro, Löwy, Biernacki, v. Limbeck, and others, I am still unable to get hold of any clinically valuable information given by the determination of alkalinity.

2. *Resistance of the red corpuscles to the influence of distilled water.* As is well known, water breaks up red cells; but if we add a certain amount of alkali, say NaCl, the cells remain uninjured. The amount of NaCl which has to be added to prevent the destruction of red cells is from 0.44 to 0.48 per cent. Under certain pathological conditions it needs either more or less of the salt to keep the cells intact, *i.e.*, they possess an increased or diminished power of resistance against the destroying influences of distilled water. The degree of concentration necessary to maintain red corpuscles intact is known as the *isotonic coefficient* of the blood as stated in terms of a given salt; 0.44–0.48 is thus the coefficient of normal blood corpuscles in NaCl, provided we do not take account of any changes in the red cells other than the giving up of their hæmoglobin. In solutions weaker than 0.44 to 0.48 per cent NaCl the hæmoglobin leaves the corpuscles; but minor changes—especially swelling of the whole cell—may occur in any solution of NaCl weaker than 0.9 per cent, so that if we desire for therapeutic purposes a solution as neutral as possible in relation to the red cells a 0.9-per-cent NaCl solution is better than a weaker one.

The resistance of the blood cells to the influence of electricity, heat, and mechanical pressure has also been investigated in various conditions of health and disease. Welch has suggested a possible clinical application of these facts. There is much, he says, for the view that the number of blood plates is an index of lowered resistance in the red cells. When resistance is lowered and blood plates increase, intravascular thrombosis—so much dreaded in chlorosis, so eagerly desired in aneurisms—is more apt to occur.

3. The amount of solids in a given quantity of blood can be determined by weighing a given amount of blood before and after six hours' drying at 65° C. Inasmuch as the hæmoglobin percentage and the specific gravity run practically parallel with the amount of solids this method has no considerable clinical value.

4. The *viscosity* of a specimen of blood may be estimated by determining the force necessary to draw it through a glass tube of a given length and diameter compared to the force needed to draw an equal volume of water through the same tube. Hirsch and Beck (*Deut. Archiv f. klin. Med.*, April 12th, 1901) have worked out an apparatus on this principle and found that judged by this test normal blood is 5.1 times as viscid as water, both being tested at 38° C. Different specimens of normal blood vary from 4.0 to 5.9 (water = 1).

PART II.

PHYSIOLOGY OF THE BLOOD.

CHAPTER IV.

ONLY such portions of our knowledge of blood physiology will be entered upon here as are necessary for an understanding of the small group of pathological changes which can be profitably investigated by clinicians. This limits us for the present to the *morphology* of the blood, its *coloring matter*, and its *density* under physiological conditions.

APPEARANCE OF FRESH NORMAL BLOOD.

I. Red Corpuscles.

(*a*) If the blood is spread thickly the blood discs are often arranged in the *form of rouleaux* (Fig. 22), which represents a form of agglutination. Adding horses' serum to human blood greatly increases the tendency to rouleaux formation, while in NaCl solution the rouleaux are not formed at all (Shattock: *Journ. of Path. and Bact.*, 1900, p. 313). The entire absence of this tendency to rouleaux formation is pathological. It is to be avoided, of course, as far as possible, as it gives us only the thin edges of the corpuscles to look at, and covers up much that we need to study. Thin spreading of the blood is therefore important.

(*b*) There is not much variation from the *accurately round shape* of each corpuscle in normal blood, except where one is indented by another. As they are moved about by the currents set in motion by the gradual drying up of the plasma, and strike against each other, they bend, double up, or indent each other like bags of jelly, but yet always have a strong tendency to return elastically to their round outline when free from pressure. Thus a corpuscle passing through a narrow passage between two leucocytes will be flattened out like a worm; but as soon as it emerges on the other side, it will be as round as before.

(*c*) The central *biconcavity* of the cell, being thinner than the rim, is lighter colored. Just how much lighter should be learned by practice so that we may detect any abnormal *pallor of the corpuscles* due to lack of hæmoglobin. Pallor is to be seen mostly in the centre of the cell, which in extreme cases seems almost transparent. This is not to be confounded with the highly refractile, glistening-white centres seen as a mark of necrosis as soon as the blood begins to dry up. A fuller description of these appearances is given in the chapter on the malarial organisms, with some forms of which they may be confounded.

(*d*) Slight *variations in size* are present among normal red discs, and here again only practice can teach us where the normal limits end and the pathological begin. Cells may be (pathologically) *all* undersized or *all* oversized, so that a standard of comparison is not always to be looked for in the preparation itself.

(*e*) If we focus carefully on a single red cell, we can usually make out a fine, wavy, so-called *molecular motion* in it. This is quite different from the active amœboid movements observed in dying cells, and from the rapid dancing of malarial pigment.

(*f*) The familiar appearance of spines all over the cells usually called "*crenation*" need not be described here (see Fig. 24, p. 79).

But it is the very earliest beginning of crenation that leads to mistakes, as when only one projection has been developed and that points toward the eye, so that a bright spot in the corpuscle is all we see.

(*g*) Unless we disinfect the skin before puncturing we must be prepared to find in fresh preparations (1) oil drops;[1] (2) epithelium; (3) particles of "dirt"; (4) small colorless motile organisms about 1 μ in diameter (Müller's "Hæmoconien," see page 58).

(*h*) We may make a rough estimate of the *number of red cells* present if we take care to spread the drop of the same thickness each time. The eye gets used to the ordinary look of a well-filled field of corpuscles and notices a look of thinness if any considerable anæmia is present.

(*i*) The *degenerative changes* to be seen in normal blood after long exposure to the air, which can get in between slide and cover, are described in detail later on. In pathological blood we may find these as soon as the blood is drawn.

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[1] In some conditions the blood really contains fat (*vide infra*, "Lipæmia").

II. White Cells.

(*a*) *The white or colorless cells* are but little different from the red in color, the latter being so nearly colorless. We first notice them either by their amœboid movements, or because they are not moved by the plasma currents, but stand like a rock round the sides of which the current of red cells is broken. They are slightly larger in most instances than the red cells; but this difference shows less in the fresh specimens where the leucocyte keeps its spherical shape than in the dried and stained preparations, where it is usually somewhat flattened. Their shape is very irregular and their edges often look tattered.

In some leucocytes the amœboid motions are almost absent These are the smallest cells, and in them a single nucleus filling most of the cell can often be seen. They are much more nearly spherical and less irregular than the larger and more active cells.

The large amœboid leucocytes are more or less granular, and in certain lights these granules look quite dark and are sometimes mistaken for bits of malarial pigment. This is especially true of the *coarse granular* cells seen occasionally; staining shows these large granules much more distinctly (=eosinophile—see below, page 61); cells of this type are the most actively amœboid of all.

(*b*) The most important point in connection with the leucocytes is their ratio to the red cells. This is estimated in fresh specimens not by any actual counting, but by reference to a standard fixed in the mind by study of normal specimens, so that any considerable increase of the white cells is noticed at once Naturally we must not judge from any one part of the slide, as the distribution of the leucocytes may be unequal in different parts of it.

III. Blood Plates.[1]

Unless the number of these elements is increased by some pathological influence, we seldom notice them at all in fresh blood. This may be because we do not work quickly enough in preparing our specimen Hayem recommends that the cover-glass be laid upon the slide before the puncture is made; as soon as the drop emerges it is allowed to run in between slide and cover by capillary attraction, thus avoiding contact with the air.[1] The blood plates are irregularly shaped, very cohesive elements, about one-half the diameter of a blood disc, usually seen clinging together in masses like zoöglœa. They are colorless and not amœboid and look like *débris.*

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[1] It is probable that the elements included under this heading comprise several different things. It is beyond the plan of this book to discuss their origin and significance, since they possess at present no clinical value.

IV. Fibrin Network.

After a specimen of fresh blood has stood for some time exposed to as much air as can creep in between slide and cover-glass, we begin to notice a network of fine straight lines in the spaces between the corpuscles. Here and there these filaments seem to radiate from a centre where irregular, colorless masses, apparently blood plates, are to be seen (Fig. 22).

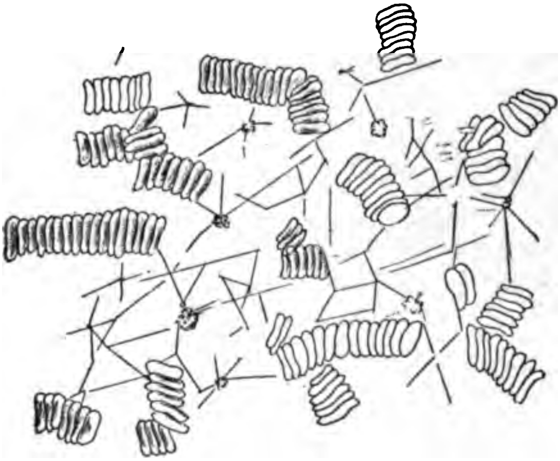

FIG. 22.—Rouleaux Formation and Fibrin Network of Normal Blood.

No stain is needed to demonstrate these fibrin threads, but a small-aperture diaphragm and very little light make them plainer.

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[1] This is a very satisfactory way if we wish to see the corpuscles as fresh and unspoiled as we can. Put a cover-glass on a slide so that the edge of one corresponds with the edge of the other, and, holding them in this position with finger and thumb, put their superimposed edges into the side of the drop as it emerges. It will run in between them by capillary attraction. Blood plates stained by Wright's method are easily seen and their number may be approximately estimated.

Their only importance is that under certain pathological conditions the fibrin network is very much increased and helps us in the diagnosis (Fig. 23). Hence it is of importance to be familiar with the ordinary closeness of the network in normal blood as a standard of comparison.

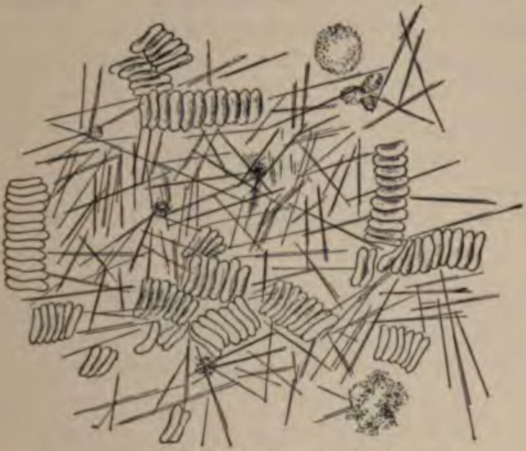

FIG. 23.—Increased Thickness of Fibrin Network.

For an account of the conditions of its increase see Chapter IX., page 114.

AVERAGE DIAMETER OF RED CELLS.

The blood under normal conditions shows considerable variations in the size of its corpuscles in the fresh state as well as in stained specimens.[1]

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[1] A method of measuring, approximately accurate, and easily applicable in clinical work is the following:

Using a camera lucida, trace on paper the divisions of a fine-stage micrometer as seen under a one-twelfth oil-immersion lens; such micrometers are usually ruled to one one-hundredth of a millimetre. Approximate accuracy in our tracing can be obtained if the process is repeated till the divisions marked in successive drawings correspond accurately one with another. Care must be taken that the paper is flat upon the table beside the microscope, and not raised on a block or otherwise; also that the part of the paper on which we draw should be perpendicularly under the centre of the mirror and not off to one side. When a drawing has been made with these precautions, we have only to divide the space between each of the lines in our drawing into ten equal parts, and we have a scale, each division of which represents 1 μ as seen

The following table (v. Limbeck) shows the results of various observers.

	Normal Limits.	Average Diameter.
Welcker	diameter = 4.5–9.5 μ	7 μ
Valentin		7 μ
Malinin		7.7 μ
Hayem	diameter = 6–8.8 μ	7.5 μ
Mallassez		7.6 μ
Laache	diameter = 6-9 μ	8.5 μ
Bizzozero		7.075 μ
Gram	diameter = 6.7–9.8 μ	7.850 μ
	Average =	7.5 μ

These differences depend partly on differences in the method of measuring (wet or dry), and partly on the fact that the age and conditions of nutrition in the persons selected make a difference. In the new-born, and to some extent throughout childhood, the normal limits of variations are wider than in adults (3.3–10.5 μ, Hayem). Sex appears to have no constant influence.

The majority of any individual's red cells are certainly about 7.5 μ *in diameter, and this may accordingly be taken as our standard* (Hayem counts twelve per cent under 6.6 μ, twelve per cent over 8 μ, the rest 7.5 μ).

NORMAL NUMBER OF THE RED CELLS.

1. At the level of the sea and in adult life the normal number of red cells per cubic millimetre is about 5,000,000 for men and 4,500,000 for women. This is frequently exceeded in vigorous, healthy persons; 6,000,000 is by no means rare among healthy young men, and higher figures are seen occasionally. Thus Hewes[1] in fifty young medical students found an average of 5,809,000 per cubic millimetre; of these fifteen exceeded 6,000,000, the highest being 6,400,000, while the lowest of the whole series was 5,120,-

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under a one-twelfth oil-immersion lens, with the tube of the particular microscope used. To use our μ-scale we have only to draw with the camera lucida any cell whose size we want to know, using always the same microscope, the same length of tube, and the same lenses, and having the drawing paper as before flat on the table and perpendicularly under the mirror. The drawing thus made is measured with the μ-scale like any other object.

With this method a cell can be measured in a few seconds and with sufficient accuracy (*i.e.*, within 0.5 μ).

[1] Transactions of the Boston Society of Medical Science, May 18th, 1897.

000. *Altitude above the sea level* raises the count invariably (see page 74).

2. The influence of *menstruation, childbirth, and lactation* is to diminish the red cells temporarily, the amount of the diminution depending not only on the amount of blood lost but on the capacity of the individual organism for blood regeneration At puberty, when sexual functions are being established, we expect lower counts than after the establishment of the function. Normal pregnancy does not affect the count of red cells.

3. The count of red cells per cubic millimetre is raised by any cause inducing *concentration of the blood*, such as profuse sweating, and is lowered by the temporary dilution of the blood after large draughts of liquid. In these changes, which are always very transient, the hæmoglobin and specific gravity in a given drop are of course increased with the corpuscles.

Vasomotor influences affecting the calibre of the peripheral vessels (hot or cold baths, exercise, etc.) may temporarily concentrate or dilute the blood by affecting the interchange of fluid between the vessels and the surrounding lymph spaces. By these processes the blood in the peripheral vessels may show an increase or diminution in the cellular elements, the hæmoglobin and specific gravity corresponding to the greater or less concentration of the blood at that point (on these points see below, page 73.)

Hayem noted that in young people especially the number of red cells varied considerably without any notable change in conditions.

4. *Influence of Nutrition on the Number of Red Cells.*

A. *After a meal*, especially when considerable liquid is taken, the blood is temporarily diluted and hence the count of red cells per cubic millimetre is diminished (v. Limbeck, Reinert). This is illustrated by the following case from v. Limbeck:

ADULT MALE, HEALTHY.

	Red Cells.	White Cells.	Hæmoglobin.
11:15 A. M.	5,530,000	7,660	98 per cent.
12 M. dinner.			
12:15 P.M.	5,320,000	6,166	
1:15 "	5,480,000	8,500	
2:15 "	4,733,000	12,000	
3:15 "	4,872,000	14,000	89 per cent.
4:15 "	4,720,000	10,830	89 "

As the white cells rise (diurnal variations, see page 91) the red fall.

Fasting, by concentrating the blood, temporarily increases the number of red cells (400,000–500,000 increase after twenty-four hours' fast).

B. *General Nutrition.*—Lean, muscular people have on the average more red cells per cubic millimetre than fat people (Leichtenstern, quoted by v. Limbeck), other things being equal.[1]

As above said, fasting (by concentrating the blood) raises the number of red blood cells, so that it is not simply hunger that gives us the *diminution* in red cells commonly found in *poorly nourished people,* but rather the influence of bad hygiene in the slums, etc.

5. *Seasons* and the *time of day* seem to have no influence in themselves. The same is true of *race* and *climate.* The only exception to this is reported in the work of E. Below,[2] who found in yellow-fever districts an average count of only 4,700,000 red cells per cubic millimetre and the diameter of the individual cell reduced to 5.9 μ on the average (7.5 μ = normal).[3]

6. *Fatigue.*—Hayem noted a loss of from 500,000 to 1,000,000 red cells per cubic millimetre in the blood of a number of farmers after a hard summer's work, the counts made in September having been compared with those of April and always found to be lower. Whether fatigue is the only cause of this diminution may be doubted.

7. *Age.*—In the new-born the number of red cells is very high for a few days (7,000,000 to 8,800,000), but falls at the end of seven to ten days (see page 445).

In the very old a certain degree of anæmia is, so to speak, physiological; but this, which like the plethora of the new-born is to be referred *not* to the fact of age but to concomitant influences, is by no means invariable. Schmaltz reports 6,766,000 red cells in a man of eighty-one and 4,816,000 in a woman of seventy-four.

Normal Number of White Cells.

The figure usually given for adults is 7,500 per cubic millimetre. This varies a good deal, according to the nutrition of the individual (see page 89) and also at different times of the day, owing to influences not explained. In animals a slight shock[1] is sufficient materially to affect the count of leucocytes; 5,000 to 10,500 may be called the normal limits. Romberg finds 9,058 as the average count in fifty-five healthy young women. There is, I believe, no evidence to show whether or not mental disturbances (fear, rage, emotion of various kinds) affect their number, but my impression is that they do. Other causes of variation will be discussed under Leucocytosis.

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[1] The influence of stasis in the obese, whose fat loads the surface of the heart, is to cause an apparent increase of red cells.

[2] "Deut. Tropenhygiene," Berlin, 1895. O. Coblanz.

[3] See also under Anchylostomiasis, page 428.

Blood Plates.

The number of blood plates is variously estimated at from 180,000–250,000 (v. Emden) to 860,000 (Kemp and Calhoun). They do not contain hæmoglobin and show no signs of a nucleus. They are the chief constituents of white thrombi. Wherever they are diminished (*e.g.*, in hæmophilia, purpura) clotting is apt to be slow, and there is reason to believe—

(*a*) That their number is an index of lowered resistance of the red cells.

(*b*) That whenever their number is much increased, thrombosis is likely to occur. In chlorosis, for instance, their number is increased and thrombosis is relatively common, while in pernicious anæmia they are diminished, and thrombosis rarely if ever occurs.

Coagulation time outside the body depends largely on the amount of fibrin and is a wholly different phenomenon from intravascular thrombosis. This is of importance in connection with the use of gelatin injections to favor thrombosis in aneurisms. An increased rapidity of coagulation outside the body is no indication of success in such cases. Blood plates are increased in chlorosis and in many cases of grave anæmia. In the severer types of many infections (measles, erysipleas, malaria) they are diminished, and in malaria they are sometimes wholly absent during the fever. In pneumonia and tuberculosis they are normal or increased. In purpura and hæmophilia they are sometimes much diminished or absent.

The physiological limits of the amount of *hæmoglobin* and of the *specific gravity* have already been mentioned. Under physiological conditions their variations follow those of the count of red cells.

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[1] Löwit: "Studien z. Physiol. und Pathol. d. Blutes," etc., Jena, 1892. Fischer.

MÜLLER'S "BLOOD DUST."

Müller[1] has described under the title of "Hæmoconien," or blood dust, a constituent of normal and pathological blood not previously noticed. This consists of small round colorless granules about the size of the finest fat drops—or about 0.25–1 μ in diameter, their size being very variable. They are highly refractile and have rapid dancing (molecular) motion, but no power of locomotion. They are insoluble in alcohol and ether, not stained by osmic acid, and take no part in the formation of fibrin. Stokes and Wegefarth,[2] who have confirmed Müller's observations, note that the "blood dust" can be seen much more clearly by the light of a Welsbach gas burner than by daylight. The latter observers present a body of evidence tending strongly to show that these bodies are the extruded granules of neutrophilic and eosinophilic leucocytes. Granules apparently identical with them can be stained in fresh specimens with eosin or Ehrlich's triacid stain in a way apparently like that of the intracellular granules.[3] They are also to be seen in pus and in hydrocele fluid.

No special diagnostic or prognostic significance has yet been attached to them, though the work of Kanthack and Stokes renders them of great interest with reference to the problem of immunity.

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[1] Centralbl. für allg. Path., etc., viii., 1896.

[2] Johns Hopkins Hospital Bulletin, December, 1897.

[3] Nicholls: Phil. Med. Jour., February 26th, 1898.

CHAPTER V.

FINER STRUCTURE OF THE BLOOD.

APPEARANCES OF DRIED AND STAINED SPECIMENS.

IN cover-glass specimens prepared and stained as above directed approximate ideas of the quantity of red cells, of white cells, and of hæmoglobin can be formed, parasites and bacteria can be seen; the whole mass of evidence based on the finer structure of the leucocytes can be obtained only in this way. The appearances of a specimen of normal blood prepared in this way are as follows:

RED CELLS.

1. With Wright's modification of Leishman's stain the hæmoglobin stains pink or yellow according to the amount of decolorization with water. With Ehrlich's triple stain the hæmoglobin takes up the orange G of the mixture, and in a properly heated specimen the red cells are of a brilliant yellow or pale orange tint. If overheated they have a feebly stained, washed-out look, while if *underheated they are more or less brown or gray.*[1]

The degree of pallor of the centres corresponds to the amount of hæmoglobin in the corpuscles, and can be gauged much more accurately in stained than in fresh preparations. The color of the edges is not much affected by pathological changes, the centres being the test. But in cases with extreme poverty of hæmoglobin the colored rim may be reduced to a mere shell and the rest may be almost completely colorless. The power roughly to estimate the amount of coloring matter in this way can be easily acquired.

An approximate idea of the number of red cells may be formed by any observer who has learned to use a uniform technique in each case and to spread the blood of a standard thickness.

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[1] This is a fruitful source of error. Many suppose that because their specimens come out too dark they must be "burnt," and so heat less. In fact the dark tint means that the specimen is not heated enough.

2. With Ehrlich's mixture the blood plates do not stain at all. With Wright's stain they are colored dark purple or red.

WHITE CORPUSCLES.

In normal blood stained by either of the methods above described we recognize the following varieties of white cells:

1. Those known as "*polynuclear*" or *polymorphonuclear neuthrophilic leucocytes*, which make up about two-thirds of all the white corpuscles of normal blood and constitute the vast majority of those found in ordinary pus. Stained by Wright's method the nucleus takes an intense navy-blue color, and a moderate amount of network structure is visible within it. With Ehrlich's stain the nucleus takes a much lighter blue color, and its edges are ill defined, so that it does not so easily catch the eye. It is very irregular in shape, and no two are just alike. One often sees two main portions with outlines about as irregular as those of the American continents, and joined by a filament as narrow relatively as the Isthmus of Panama. The different parts of the nucleus often seem to be wholly separated from each other, but this is very rarely if ever the case. Careful focussing brings out fine filaments joining the apparently separated pieces. The windings and twistings of the nucleus suggest comparisons to the letters Z, S, or E.

In the protoplasm of the cell around the nucleus fine granulations can be demonstrated which take a variety of shades of pink with Wright's stain, and with Ehrlich's a violet or purple. They are very small and irregular in shape, contrasting with larger and more spherical granules of the eosinophile. Between them can be seen in most cases a pinkish stained background of cell substance. With the lower powers of the microscope they seem to fuse together into a diffuse pinkish or purplish mass.

The term "neutrophilic" is not strictly accurate, since the granules can be stained (though more faintly) with eosin, but they are most distinct when stained with a differential acid mixture like Ehrlich's "triacid," which contains both an acid and a basic dye. There is some evidence for believing that these granules have when young a basic affinity, gradually changing to an acid affinity as they mature.[1]

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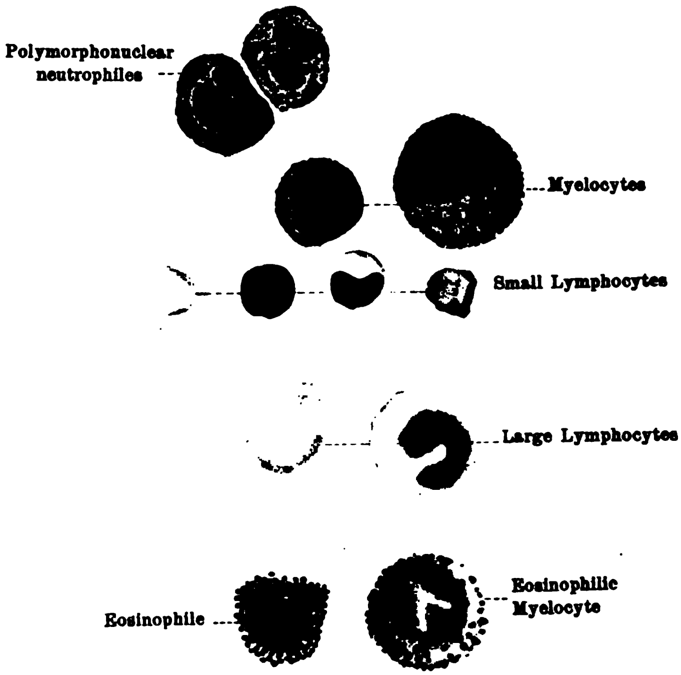
[1] In infectious diseases and grave anæmias the granules of the polynuclear cells may altogether lose their staining affinities or large oval basophilic dots

Examination of the Blood.

PLATE I.

Fig. 1. **Varieties of Leucocytes.**



The Malarial Organism.

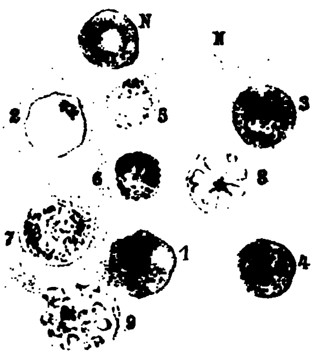


Fig. 2.

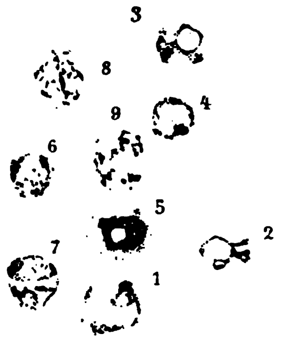


Fig. 3.

R. C. Cabot fec.

Lith. Anst. v. E. A. Funke, Leipzig.

PLATE I.

FIG. 1.—(*a*) *Polymorphonuclear Neutrophiles.* Note the varieties in size and shape of granules, the irregular staining of the nuclei, the light space around them, their relatively central position in the cell.

(*b*) *Myelocytes.* Note identity of granules with those just described; the even, pale stain of nuclei; their position near the surface (edge) of the cell. The two cells figured indicate the usual variations in the size of the whole cell.

(*c*) *Small Lymphocytes.* In the cell at the left note transparent protoplasm; in the cell next to it note *very* pale pink of protoplasm around nucleus which is deeply stained, especially at the periphery. The next cell has an indented nucleus; its protoplasm relatively distinct. The cell on the extreme right shows no protoplasm and is probably necrotic. In all note *absence of granules* with *this* stain. With basic stains a blue network appears in the protoplasm.

(*d*) *Large Lymphocytes.* Note pale-stained nuclei and protoplasm, irregularity of outline; indented nucleus in one. Every intermediate stage between these and the "*small*" lymphocytes occurs, and the distinction between them is arbitrary.

(*e*) *Eosinophile.* Note irregular shape, loose connection of granules, their copper color, their uniform and relatively large size, and spherical shape.

(*f*) *Eosinophilic Myelocyte.* Note similarity to (*b*) ordinary myelocytes except as regards granules. Color of granules may be as in (*e*) ordinary eosinophile.

All the above were stained with the Ehrlich triacid stain, and drawn with camera lucida. Oil-immersion objective one-twelfth and ocular No. iii. (Leitz).

FIG. 2.—*Malarial Parasites in Fresh* (*Unstained*) *Blood* (Tertian Forms). *N*, *N*, normal red corpuscles; 1, red cell containing *hyaline body;* 2, 3, 4, 5, successive stages in the development of the parasite, showing acquisition of pigment; 6, 7, full-grown parasites, the corpuscle no longer visible; 8, beginning of segmentation; 9, segmentation. In 6 and 7 note brownish blur behind the pigment dots. Drawn as in Fig. 1.

FIG. 3.—*Tertian Parasite Stained with Eosin and Methyl Blue.* The remains of the corpuscle containing the parasite stain pink, the parasite blue, and its pigment black. The stages of growth correspond with the numbers attached. Note in Figs. 1, 2, 3, and 4 the shape of the parasite, shown better than in fresh specimen.

[Owing to a mistake the cells in Fig. 3 are not drawn according to a single scale and their relative sizes must be disregarded.]

2. *Lymphocytes.*—With Wright's stain the nucleus, which is about the size and shape of a red corpuscle, stains deep purplish blue (see Plate A). Around it is a narrow rim of protoplasm, which takes a robin's-egg-blue tinge. As a rule this rim shows no granules, but occasionally a few blue or pink dots may be seen upon it. With Ehrlich's triple stain the nucleus of lymphocyte is colored very pale blue in the majority of instances, so that the cell often escapes notice in hasty differential counts. The protoplasm may be altogether unstained, or may be of a bluish tint, still paler than that of the nucleus (see Plate I).

Cells of the type just described vary in size from that of a red corpuscle, or slightly smaller, up to two or three times that size. In the larger forms the nucleus may be eccentric or indented and the protoplasm rim wider. One often sees in the protoplasm of these forms pink, purple, or dark-blue granules, which are of various sizes, but usually scanty. Some of the large forms have a protoplasm considerably darker in color than that of the small lymphocytes, and at times the granules are so numerous that it is difficult to distinguish the cells from myelocytes.

Occasionally the nucleus is more or less deeply indented at one side (Ehrlich's "transitional forms").

Within the group of cells just described most competent observers distinguish two types, one called "*lymphocytes proper*" (large or small) and the other "*large mononuclear cells.*" I think there is good reason to believe that this distinction is correct, but as no clinical importance has ever been attached to the so-called large mononuclear cells, and as they make up in the great majority of cases but a few per cent of all the leucocytes, it seems to me best at the present time to include them for practical purposes within the lymphocyte group.

3. *Eosinophiles.*—With Wright's stain the nuclei are stained light blue or lilac, with a vague intranuclear structure. They are polymorphous, like those of the neutrophiles, but with a looser structure. The granules, which are about 1 μ in diameter and roughly spherical or ovoid in shape, take with Wright's stain a brilliant eosin tint, while around them the protoplasm is very pale blue. With Ehrlich's stain the granules are copper-colored or brown, the nucleus is very pale blue, the protoplasm unstained.

may appear among the normal granules. (Hirchfelt: Berl. klin. Woch., July 22d, 1901.)

These cells are more easily injured by the technique of spreading the film than is any other variety of leucocyte, and are often found broken, their granules scattered about the fields.

4. *Mast Cells.*—One of the striking features about Wright's stain is the prominence which it gives to the mast cells, which, with Ehrlich's stain, usually escape notice altogether. They are about twice the diameter of a red cell. Their nucleus has very vague outlines, but seems usually to be polymorphous. Over and around it are scattered granules larger even than those of an eosinophile and of an intense blue color, sometimes almost black. They may be very numerous, practically obscuring the nucleus, or scattered thickly about the margin of the cells. Occasionally they are distinctly ovoid and plum-colored.

Summing up, we find it most convenient to divide the leucocytes of normal blood into four varieties:

1. Polynuclear or polymorphonuclear neutrophiles.
2. Lymphocytes—large and small (including the so-called "large mononuclear" forms and Ehrlich's transitional cells).
3. Eosinophiles (polynuclear).
4. Mast cells.

Terms.

No one can feel more unsatisfied with the terminology used in this book than the writer. It rests partly on a theory of the origin of the cells ("lymphocytes"), partly on the properties of the nucleus ("polymorphonuclear"), and partly on affinities for aniline dyes ("neutrophile"—"eosinophile").

All that can be said for it is that it discards certain very misleading names like "splenocyte" (a term applied by some to the large lymphocytes according to the now exploded theory that they come from the spleen), or like "small mononuclear," to designate cells not rarely polynuclear.

Origin of the Different Varieties.

Two groups may be distinguished:

- I. The myelogenous group (from the bone marrow).
  - (*a*) Polymorphonuclear neutrophiles.
  - (*b*) Eosinophiles.
  - (*c*) Mast cells.
  - (*d*) Large mononuclear cells (Ehrlich)?

II. The lymphogenous group (from adenoid tissue).	Lymphocytes of all sizes.

Except within Group II. no transitions between the different varieties of circulating leucocytes are recognized.

Normal Percentage of Each Variety.

In the blood of healthy adults the proportions of the different varieties above described are the following:

(*a*)	Small lymphocytes	20–30	per cent.
	Large "	4–8	"
(*b*)	Polymorphonuclear neutrophiles	62–70	"
(*c*)	Eosinophiles	$\frac{1}{2}$–4	"
(*d*)	"Mast cells"	$\frac{1}{40}$–$\frac{2}{10}$	"

(*a*) In infancy the percentage of lymphocytes is much larger (forty to sixty per cent) and the polymorphonuclear neutrophiles are only eighteen or forty per cent.

In a variety of debilitated conditions not usually thought of as definite diseases, the percentage of lymphocytes is comparatively large and that of the polymorphonuclear cells small.[1] The general vigor and health of the individual can sometimes be estimated simply from the leucocytes. Persons calling themselves well, but never vigorous or active, may show no more than fifty per cent of polymorphonuclear cells, the lymphocytes running up to forty, fifty, or even seventy-five per cent. In an unmarried woman of twenty-nine, suffering from no discoverable organic disease, I found one day among 1,200 leucocytes 74.9 per cent of lymphocytes with only 25 per cent of polymorphonuclear cells. The total leucocyte count was 6,000 per cubic millimetre. Two weeks later the percentages were normal, although no change had been observed in the patient's (debilitated) condition. She is now well and married.

Not all cases of debility show this change, and we are not yet in a position to say under just what conditions it occurs. It certainly is not peculiar to tuberculosis, as Holmes has supposed. Presumably the conditions are such as decrease the functional activity of the marrow.

(*b*) Changes in the percentage of neutrophiles will be discussed later.

(*c*) The percentage of eosinophiles often changes in a way hard to explain. Their increase or decrease in the circulating blood does not follow that of the polymorphonuclear neutrophiles—in fact is often inversely proportional to it, and the eosinophiles may be markedly increased in a blood otherwise normal, for reasons wholly unknown to us.

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[1] This change is usually dependent on an *absolute* diminution in the myelogenous cells.

The eosinophiles and "mast cells" may be pictured as comparative strangers, though not intruders in the circulating blood. They are thus intermediate between the regular inhabitants (lymphocytes and neutrophiles) and the variety next to be mentioned, which are real intruders—*i.e.*, almost never found in normal blood. These are the

MYELOCYTES.

The larger portion of the leucocytes of the marrow is made up of mononuclear neutrophiles, a type of cell not yet described, and differing from any variety found in normal blood, although it has many points of resemblance to the polymorphonuclear neutrophile, and is, in fact, the same cell in an early stage of growth. I describe it here because it is peculiar to no one disease and is an occasional visitor of the blood in various diseased conditions, and in conditions on the borderland between the pathological and the physiological (starvation, muscular fatigue).

The myelocyte (see Plate I. and Plate B.) is most easily recognizable if stained by Ehrlich's methods. With Ehrlich's triple stain it appears as a spherical cell nearly filled by a large, pale-stained nucleus immersed in neutrophile granules. One sees at once how little it differs from the large lymphocytes (simply in having granules) and from the polymorphonuclear neutrophile (only in the shape of its nucleus). I have called the granules neutrophilic, and this is true of the great majority of them in most cells. But as Ehrlich has recently pointed out, there is a great deal of variation in the staining affinities of different granules, side by side, in the same cell. In some granules (according to Ehrlich the younger ones) "there is prominent a basophile portion which becomes less and less marked as the cell grows older." Such granules take with Wright's stain a bluish tint. Others near them (older?) are violet, while others again are nearly pink. In the polynuclear neutrophile these basophile affinities are much less marked, but even in them considerable differences may be made out between the tints of adjacent cells and of adjacent granules in the same cell. In size and shape the myelocyte granules are like those of the polynuclear cell. The nucleus, by which we chiefly distinguish the myelocyte, shows none of the twists and turns characteristic of the polymorphonuclear neutrophile, but is usually spherical or egg-shaped, and is in close contact with the cell wall for a comparatively large portion of its extent—*i.e.*, if egg-shaped it is placed eccentrically.

Not infrequently the nucleus shows signs of old age (vacuoles) or of mitosis, for occasionally we find two nuclei at the poles of the cell.

Size of Myelocytes.

All the older accounts of the myelocyte speak of it as a very large cell, the largest variety of leucocyte ever seen in the blood.

This is true of many of them; diameters of 18–21 μ are not uncommon, but we also find them of *every* other size down to 10–11 μ diameter—that is, down to the size of a lymphocyte. This holds both for the myelocytes in the circulating (leukæmic) blood and for those in the marrow. No distinction from other varieties of leucocyte can be based on size alone, unless we say their *average* size is greater than the average size of the leucocyte. Perhaps the following table may be of interest:

Average diameter of 100 myelocytes = 15.75 μ.
“ “ “ 100 polymorphonuclear neutrophiles = 13.50 μ.
“ “ “ 100 “large” lymphocytes = 13 μ.
“ “ “ 100 eosinophiles = 12 μ.
“ “ “ 100 “small” lymphocytes = 10 μ.
“ “ “ 100 red corpuscles (normal) = 7.5 μ.

EOSINOPHILIC MYELOCYTES.

Under the same conditions which favor the appearance of the ordinary (neutrophilic) myelocyte, we often find a small number of cells identical with them in all respects, except in possessing eosinophilic in place of neutrophilic granules. Such cells are found in abundance in the marrow, and this fact, together with the resemblance to the ordinary myelocyte both in morphology and in the conditions of their occurrence, seems to me to justify the term *eosinophilic* myelocyte. In them as in all myelocytes there is a wide variation between the staining affinities of different granules, some being much darker than others.

So far I have described the *type cell* of each variety. As we should expect, atypical forms are numerous. Some of the commoner ones are as follows:

I. DEGENERATED LEUCOCYTES.

Frequently in leukæmia and occasionally in other conditions one sees leucocytes apparently moribund. That they are not ordinary artifacts is shown by the fact that they are not found in normal blood treated by the same technique that reveals them in the blood and in hardened blood clot of leukæmic cases, as well as by the fact that Botkin and others have produced similar appearances by keeping the leucocytes a few days in an aseptic state.

The commonest forms of degenerated leucocytes are:

1. A homogeneously stained mass looking like a washed-out, structureless nucleus that has lost its protoplasm and become ragged at the edges (karyolysis).
2. The same intensely stained.
3. Vacuolization of the nucleus or of the protoplasm.

All these forms of degeneration affect chiefly the lymphocytes and large mononuclear forms. In the granular leucocytes we see all stages of breaking up; the granules are scattered about the field and the nucleus is pale, structureless, and deformed.

II. TRANSITIONAL NEUTROPHILES.

Cells on the borderland between the "marrow cell" and the "polymorphonuclear leucocyte," the nucleus having some of the characters of each variety (see below, page 103).

III. TURCK'S "STIMULATION FORMS."

These cells are also described by Engel as "mononuclear cells" and very recently by Weil as "non-granular myelocytes."

Weil's description conveys the salient points in the appearance of this cell. It looks like a myelocyte whose granules have been fused into a smooth homogeneous band of color around the single spherical or ovoid nucleus. The protoplasm is always homogeneous and deeply stained; there is, however, a good deal of variation in the tint in different cells. In some it is purple, in others violet or brown. In leukæmia they are often counted as myelocytes or as large lymphocytes by unpractised observers.

They appear in various diseases associated with *stimulation of the bone marrow*, *i.e.*, grave anæmia and all conditions associated with leucocytosis (see below, pages 102–103).

Other rare varieties will be mentioned under Leukæmia.

PART III.

GENERAL PATHOLOGY OF THE BLOOD.

CHAPTER VI.

UNEQUAL DISTRIBUTION OF BLOOD—POLYCYTHÆMIA—DILUTION AND CONCENTRATION OF THE BLOOD.

1. Unequal Distribution.

How far is the single drop used for blood examination typical of the whole?

It has been experimentally proved that specimens of the blood of the smaller venous and arterial twigs do not differ from each other materially in corpuscular richness. Capillary blood is slightly richer in corpuscles than that either of veins or of arteries. But as capillary blood is everywhere of the same corpuscular richness, we may consider one capillary network or set of venules as typical as another, provided our technique is good—that is, provided lymph is not squeezed into the drop by strong pressure. It is indifferent, therefore, so far as accuracy is concerned, whether the drop of blood be obtained from one or another part of the body. All standard estimates of the number of corpuscles per cubic millimetre of normal blood refer to capillary blood.

2. Local or Peripheral Polycythæmia.

So far we are speaking of normal conditions. It is a familiar fact, however, that the vessels of a given part of the body can be overcrowded with blood, *e.g.*, by the use of an Esmarch bandage. A drop taken from such a part would certainly not be typical. Now as the same effect can be produced by a variety of diseases, under these conditions we must modify considerably any inferences made from examination of a single drop.

Such conditions, entailing a false polycythæmia or apparent increase in the number of corpuscles, are:

Any disease involving either (*a*) general cyanosis or (*b*) cyanosis of the part from which the drop of blood is drawn.

(*a*) *General cyanosis* results from cardiac insufficiency (valvular or parietal disease of the heart itself, blocking of the lung circulation by emphysema or thrombosis), from insufficient aëration of the blood (pneumonia, congenital malformation of the heart), interference with the heart's action by pressure of tumors, effusions (pericardial, pleural, peritoneal), or enlarged organs (liver, spleen), or from vasomotor disturbances. It is evident that some of these conditions (*e.g.*, congenital heart disease) may not involve any peripheral stasis at all, and in the absence of this it is not easy to account for the increased number of corpuscles in the drop. Whatever the explanation may be, there is no doubt of the fact that general cyanosis from any cause whatever produces an increase of cells in a drop such as we usually examine..

The cases of cyanosis which I have classed under "cryptogenetic polycythæmia" (for want of a better name), cases in which, in the absence of disease in any organ, the skin and mucous membranes are persistently and markedly bluish, are not very uncommon. I have seen three such, all in stout, elderly women. In one the cells in a drop of blood from the ear, finger, or toe were more than *double* the normal number (see page 71.)

(*b*) *Local Cyanosis.*—The pressure of a tumor, or any other hindrance to the circulation of any part, may give a similar increase in the number of corpuscles in a measured amount of blood from that part. In paralyzed patients the count may be higher on the paralyzed side. In markedly cyanotic patients the count of red cells may be notably above normal, and we must make allowances. Error is more likely to arise when we have cyanosis in a person whose blood is poor in red corpuscles. The combination of these two factors may give us a normal blood count and lead us to overlook the anæmia. Thus a person might have really a severe anæmia and yet the count of red cells be actually above the normal. This element of stasis should never be lost sight of. Many high counts reported in pneumonia or hysteria are to be explained by abnormalities not of *production* or *destruction* but of *distribution* of the blood cells.

With these exceptions the drop of blood taken at the periphery is typical. We have next to consider some *general* conditions under which a person's whole blood may be inferred to be abnormal from the findings in a drop taken from the periphery. Consideration of *special* diseases will follow later.

Temporary increase or diminution in the amount of fluid within the vessels can be brought about not only by a change in the mechanical conditions of pressure and osmosis, but by any influence affecting the tone of the peripheral vessels. We have then:

Temporary Serous Plethora or Dilution of the Blood.

(*a*) From transfusion of fluid in large amounts or its ingestion by mouth or rectum.

(*b*) From decreased blood pressure, as in acute failures of compensation in cardiac disease.

(*c*) From vasomotor dilatation.

As an example of this last Grawitz reduced the specific gravity of the blood from 1041 to 1038.7 within eight minutes by the inhalation of nitrite of amyl. This decrease of specific gravity can only mean an increased amount of watery constituents in the blood, as there was no evidence of any destruction of the heavier elements of the blood, and only water (and chlorides) pass through the vessel walls easily. In the above case the specific gravity was again at 1041 within a few minutes.

Polycythæmia.

The red-faced persons popularly known as "full-blooded" show no abnormalities in their blood discoverable by any means of investigation known to us. The condition is probably dependent on the presence of a rich capillary network near the surface of the skin, or on a dilatation of individual venules and arterioles at the periphery. Such a person may be markedly anæmic without any considerable changes in the color of the face. The fact that people of such complexion often end their lives with a ruptured cerebral artery is due presumably to the circumstance that "high living" produces in the same individual dilated peripheral capillaries and weakened arterial walls.

Examples of what seems more likely to be a true polycythæmia are as follows:

(*a*) In cases of severe anæmia which recover, the blood regeneration may attain such vigor that the number of red cells shoots *temdorarily* up *above* normal, even as high as 7,700,000.

(*b*) The same condition can be temporarily produced by transfusion of actual blood from one individual to another. It lasts but a few days as a rule.

(*c*) Some cases occur without any known cause. In one such case which came to autopsy (death from cerebral hemorrhage) the internal organs were as deeply engorged as the periphery of the body. Similar cases—often associated with splenic enlargement—have been reported by Vaquez, Osler (Trans. Assn. American Physicians, 1903), by McKeen (*Boston Med. and Surg. Jour.*, June 20th, 1901), by Saundby and Russell (*Lancet*, 1901, i., p. 515) and by Hall (*Amer. Med.*, June 27th, 1903). The cases of the following table are apparently of this type.

TABLE I.—CRYPTOGENETIC POLYCYTHÆMIA.

Age.	Sex.	Red cells.	White cells.	Hæmoglobin.	Remarks.
29	....	8,484,000	15,000	85	February 5. Polynuclear, 84.6; lymphocytes, 13.8; eosinophiles, 1.6.
		....	17,600	....	February 8. Polynuclear, 90.4; lymphocytes, 8; eosinophiles, 6; myelocytes, 1.
56	....	6,240,000	10,000	65	First day.
		4,680,000	5,600	70	Eighth day.
53	F.	11,352,000	8,300	105	December 6.
		9,260,000	....	105	December 7. After walking.
		10,060,000	....	110	
			10,400 *a.c.* 11,700 *p.c.*	....	December 11.
		10,230,000	8,800	110	December 17. Polynuclear, 77.25; lymphocytes, 18.75; eosinophiles, 2.75; myelocytes, 1.25; microblasts, 2; normoblasts, 2. Few mast cells.
29	M.	8,484,000	17,600	....	Polynuclear, 90; lymphocytes, 8; eosinophile, 1; mast cell, 1.

The polycythæmia of the new-born, of high altitudes, and of phosphorous poisoning will be discussed later.

Concentration of the Blood.

It is obvious that influences opposite to those producing temporary full-bloodedness will produce temporary lack of fluid within the vessels. So acute diarrhœa, purgation, deprivation of liquids (as in starvation), rapidly accumulated serous effusions, profuse vomiting or sweating (by skin and lungs) produce a temporary *concentration of the blood* by draining out its diffusible elements (water chiefly) (see Table II.). All these influences are transitory. More permanent drains on the system, like chronic diarrhœa, diabetes insipidus or mellitus, or long-standing suppurations, show no evidence of lessening the volume of blood in the vessels. They drain albumin out of the serum and corpuscles and so decrease the weight of the blood (see below, page 78), but the blood volume is not changed. Indeed, any influence has to work very quickly in order to concentrate the blood, for in an astonishingly short time the other tissues repay the vessels their loss of fluid and the normal blood volume is restored.

The same temporary effects can be produced by influences constricting the vessels (cold, pain, suprarenal extract), and a concentration of the blood results which lasts a few minutes or hours.[1]

In all these interchanges of contents between the blood-vessels and the other tissues it is, as above said, the watery elements chiefly that change. The red cells are not affected by the give-and-take of the vessels and tissues, and although cold produces in the peripheral circulation an increase in the number of white cells greater than can be accounted for by simple concentration, the weight of evidence seems to be against any new production of cells and in favor of a change only in distribution, the white cells accumulating at the periphery.

Now as the number of cells is not affected by these temporary variations in the volume of liquid within the vessels, it follows that the number to be counted in a cubic millimetre, though typical of the whole blood *at that time*, is not to be reckoned from in the ordinary way. For example, after a severe diarrhœa or in phthisis after a night-sweat the blood may be temporarily so concentrated that we find 6,000,000 or more red corpuscles per cubic millimetre. Under normal conditions of the blood mass we should infer from such a count that the body contained one-sixth more red corpuscles than usual. Here obviously it means only (if anæmia is absent) that the blood mass is reduced one-sixth by concentration. It is only in such sudden reductions of blood volume that we can measure the amount lost by this method. Long-standing causes of drain on the plasma might at any time act as destroyers of red corpuscles as well, through the changes in the nutritive fluids in which they live.

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[1] Oliver has shown recently (Lancet, June 27th, 1896) that any influence causing rise of blood pressure will slightly concentrate the blood. Thus raising the arm over the head and holding it there by muscular effort slightly concentrates the blood in that arm. Electrical stimulation or massage of the arm has the same effect. *Lowering* blood pressure, as when the arm is supported *passively* over the head, dilutes the blood. This confirms the results of Mitchell (Med. News, May, 1893) and of Chéron (Comptes Rend. de l'Acad. d. Sciences, 1896, No. vi.).

Further, it is only when we know the number of corpuscles just before the sudden drain on the plasma comes that we can measure the amount of plasma lost by the amount of *apparent* increase in the red cells. Stasis and any other cause that heaps up corpuscles at the periphery must also be excluded before we can judge of the loss of plasma in this way.

The conditions of an abnormal concentration of the blood are those already alluded to as temporarily sucking away its watery constituents, namely:

(*a*) Watery diarrhœa, especially in cholera and other acute diseases accompanied by diarrhœa.

(*b*) Large and rapidly accumulating serous effusions (slow accumulations would give time for the blood to take up water from the tissues and make up for its loss).

(*c*) Profuse sweats.[1]

(*d*) Persistent vomiting or starvation of liquids (see Table II.)

(*e*) Increased blood pressure (exercise, massage, electricity).

Blood already lacking in red cells, if suddenly concentrated by such a loss of fluid, might deceive us into supposing it normal, because the number of cells in a cubic millimetre might be normal. *In the presence, therefore, of any such reason for concentration of the blood, we should always modify our ordinary methods of inference from the blood count.* For example, v. Limbeck records a case of hepatic cirrhosis with ascites in which before tapping the ascites the count of red cells was 3,280,000 per cubic millimetre. Within twenty-four hours after tapping there were 5,160,000 cells per cubic millimetre, the reaccumulation of the ascitic fluid going on so fast that the blood was unable to adjust itself and became overconcentrated. A careless observation might have inferred a great gain in the corpuscular richness of the whole blood, when in fact not a corpuscle had been gained, and those present had probably grown poorer in albumin.

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[1] Mayer (Zeitsch. f. dietet. u. phys. Therap., 1902, vol. vi., Hft. 7) finds that hot-air baths produce a transient increase in the hæmoglobin and in the leucocytes. Hot-water baths had no effect on the leucocytes and slightly diminished the hæmoglobin.

The combination of hot baths and hot drinks produces in children, according to Hannes (Centralb. f. in. Med., 1901, p. 823), a slight leucocytosis lasting about an hour.

TABLE II.—STARVATION.

Case.	Age.	Red cells.	White cells.	Hæmoglobin.	Remarks.
1	23	12,000,000	10,000	120 +	Stowaway. Ten days without food.
2	2	8,780,000	....	......	Two weeks' starvation after caustic potash stricture of gullet.

It remains to speak of two other conditions in which what *appears to be* a true polycythæmia is found:

1. In persons living at high altitudes.
2. In persons suffering from phosphorus or CO poisoning.

1. The Blood in High Altitudes.

The polycythæmia of those living at high altitudes increases the higher one goes. Köppe[1] gives the following table:

Place.	Height above sea level.	Red cells.	Author.
Christiania	O	4,974,000	Laache.
Göttingen	148 metres	5,225,000	Schafer.
Tübingen	314 "	5,322,000	Reinert.
Zürich	414 "	5,752,000	Stierlin.
Auerbach	425 "	5,748,000	Köppe.
Reiboldsgrün	700 "	5,900,000	"
Arosa	1,800 "	7,000,000	Egger.
The Cordilleras	4,392 "	8,000,000	Viault.

This change takes place within two weeks of the time of taking up residence in a high place, and independent of any change in diet or manner of living; even within twenty-four hours there may be a gain of 1,000,000 red cells per cubic millimetre. Phthisical patients' blood is more affected than that of healthy persons. Animals show similar changes. The hæmoglobin is also inconsiderably increased, although it lags somewhat behind the corpuscles. Solly (*Phil. Med. Jour.*, 1900, vol. i., p. 1074) reports that the increase so marked in newcomers partially disappears after two or three years' residence, while the blood of natives of the same high altitude is midway between normal and that of persons who have lived there but a few years.

The corpuscles are often deformed and undersized during the

[1] Münch. med. Woch., 1890, No. 41.

earlier weeks of the change; but their volume, as determined by the hæmatocrit, is not increased, and nucleated forms are not found.

Later the poikilocytes and microcytes vanish and the hæmoglobin percentage rises so as to correspond with the increased count of red cells.

On returning to low land, the blood returns within a short time to its normal condition.

Many explanations have been offered for this interesting phenomenon, the most reasonable, I think, being that which considers it a vasomotor phenomenon, due to lowered barometric pressure.

2. Phosphorus and CO Poisoning.

The polycythæmia of acute phosphorus poisoning may reach as high as 8,650,000. This may be partly explained by concentration due to the occurrence of vomiting; but in some cases the increase seems out of proportion to the amount of vomiting.

With illuminating-gas poisoning there is usually no vomiting to speak of, and the cause of the marked increase in the red cells is unknown. Von Limbeck in two cases of CO poisoning showed respectively 6,630,000 and 5,700,000 red cells. Münzer and Palma[1] record 5,700,000. The white cells are also increased (see page 413).

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[1] Zeit. f. Heilk., vol. xv., p. 1.

CHAPTER VII.

ANÆMIA AND HYDRÆMIA.

1. ANÆMIA.

Definition.—*A deficiency in corpuscle substance, i.e.*, a deficiency in red corpuscles, in hæmoglobin, or in both,[1] with or without changes in the total volume of the blood.

It is important to bear in mind that the color of the skin is not a safe guide in judging whether a person is anæmic.

The most striking example of the fallacy of judging of anæmia by the color of the skin and mucous membranes is in the so-called "*tropical anæmia.*" Practically all persons belonging to white races who take up their residence in the tropics acquire after a time an extreme pallor of the skin and mucous membranes, and this appearance has usually received the title of "tropical anæmia." It turns out, however, from the careful studies of several different investigators, that the blood of such persons shows absolutely no anæmia or other variation from the normal.[2]

We are to judge of anæmia, then, solely by the blood examination.

Distinction between Primary and Secondary Anæmia.

In one sense all anæmia is secondary. It is due to some cause, a symptom in a chain of events. But in some cases we know the cause and in some we do not.

(*a*) *Primary anæmia is that in which the causal factors are either entirely unknown or are apparently insufficient to produce so severe a disease.* This division, like most of our statements about the blood, is a rough-and-ready one, held provisionally until a better classification is discovered. It has a certain utility if not used with any less simple meaning than that given above.

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[1] This is a clinical definition and makes no attempt to go to the root of the matter. I have little doubt that chemical or other changes in the serum are the cause of the corpuscular changes, which only mirror the deeper disease. But these chemical changes are as yet so little understood that we have to judge of their presence chiefly by their effect on the corpuscles.

[2] So far as present methods of examination go.

There is no good evidence that there are any primary diseases of the blood-making functions. A case of secondary anæmia is one in which we have an obvious cause such as hemorrhage or malaria for the loss of corpuscle substance. Remove the cause and the anæmia ceases. Sometimes, however, after removal of the cause, *e.g.*, after cure of a case of syphilis, the anæmia set agoing by the syphilis persists. On the other hand, there are few patients with "primary" anæmia who cannot recall some event in their past lives sufficient to account for *a certain grade of anæmia* (*e.g.*, a nervous shock, a hemorrhage, an attack of tertian malaria). Yet if the anæmia that occurs after so slight a cause is of the pernicious or fatal type, we may fairly call it "*primary.*" By this we mean that though the "cause" assigned might produce *some* anæmia, it was not sufficient to produce *this* fatal anæmia and has presumably little or no connection with it. "Primary" means not the absence of *any* cause of anæmia in the history, but the absence of any *sufficient* cause so far as is known.

An attack of tertian malaria or a history of bleeding piles does not cause fatal anæmia in 999 out of 1,000 people who have such a history. In the 1,000th it is a case of *post hoc* and not *propter hoc.* Given the unknown cause that *does* lead to "primary" anæmia, and it might be that a pregnancy, a nervous shock, or the presence of intestinal parasites would act as the straw that breaks the camel's back; but *the important causal factor is the unknown factor.* Evidence is accumulating in support of Hunter's view that pernicious anæmia is due to excessive blood destruction produced by toxic substances absorbed from the gastro-intestinal tract. Chlorosis is now generally believed to be a disease representing defective blood formation. But we are still in the realm of theory in these matters.

It is true that in the majority of cases we can tell from the blood examination alone whether a case is without known cause (= "primary") or symptomatic (= "secondary"). But there appear to be enough exceptions to this rule to make us cautious about stating it as a law.

ANÆMIA =	**Primary** =	**Chlorosis.** **Pernicious anæmia.**	To be discussed under Special Pathology of the Blood, Chapter VII.
	Secondary.		

Secondary Anæmia.

I. *First Stage.*—I defined anæmia above as *a diminution in corpuscle substance.* In the milder types of this condition the number of red corpuscles is not diminished at all, but the individual cell is small, pale, and of light weight, through loss of nitrogenous matter. This is appreciated:

(*a*) As a lack of coloring matter.

(*b*) As a lowering of the specific gravity.

In the mildest grades of secondary anæmia there are no further changes.

The lack of coloring matter is usually not present in every cell, as is seen in the stained specimens. Some are very pale at the centre, while others are well stained.

II. *Second Stage.*—Usually the next changes to appear are, like those already mentioned, *qualitative,* the number of red cells still remaining normal or approximately so.

The individual cell as seen in fresh preparations is more or less deformed and varies from its normal diameter, dwarfed forms usually being commoner than the giant forms. These variations in size and shape are sometimes termed "*poikilocytosis,*" and the dwarf and giant forms are called respectively microcytes and macrocytes.

Maragliano[1] has included the above changes, together with others about to be described, under the heading of

Necrobiosis in the red corpuscles, attributing them to a pathological condition of the serum.

The changes united under this heading may be divided for convenience' sake into

(*a*) Endoglobular changes.

(*b*) Poikilocytosis and crenation.

(*c*) Changes in staining properties.

(*d*) Changes involving motility in the corpuscle as a whole, or in parts of it.

(*e*) Decrease in the average diameter of corpuscles with loss of the power to form rouleaux.

All these changes may be watched in normal blood outside the vessels, as necrosis gradually comes on from contact with the air.

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[1] XI. Cong. f. Inn. Med., Leipzig, 1892.

Under pathological conditions the same changes may occur *outside the body*, but more quickly than usual (as other diseased tissues decompose more quickly after death than those of a sound man suddenly killed), or *inside the body*.

(*a*) *Endoglobular Changes* (see Fig. 24, *a*).—These consist in the appearance of clear hyaline spaces of various shapes within the corpuscle, round triangular, rod-shaped, etc. In the fresh specimen they change their shape rapidly and continually; in dried and stained specimens they appear as sharply outlined light spaces in the corpuscle. In normal blood these changes occur after thirty to seventy minutes outside the vessels. In some pathological conditions specimens show them the instant the blood is collected, and presumably they were present before it left the vessels.

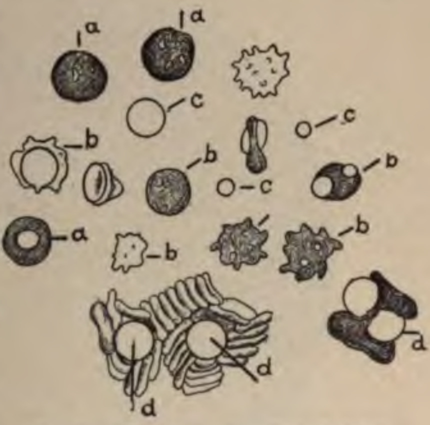

FIG. 24.—Degenerative Changes in Red Cells.

(*b*) *Crenation and Poikilocytosis* (Fig. 24, *b*).—What we know as crenation in the corpuscles is probably the same sort of process which, occurring within the vessels, we call poikilocytosis. A lump rises at one or more points in the corpuscle, becomes more pointed, and gradually the whole cell acquires amœboid motions, assuming in succession the various shapes with which we are familiar in poikilocytes. Hayem has minutely described four types of motion in the red cells of anæmic blood.

1. General amœboid motion of the whole cell.
2. Vermicular motion of flagella-like prolongations.
3. Oscillating motions, especially in small light cells.
4. Pseudo-parasitic motion.

(*c*) The pointed projections may break off and move about actively in the plasma. These motions, as well as the preceding amœboid movement of the whole corpuscle, are to be explained as irregular contractions of the necrobiotic protoplasm, similar in a general way to the actions of a hen after its head is cut off. These motions are not to be confounded with the finer Brownian or "molecular" movement to be seen in any healthy cell. The small bits broken off (Fig. 24, *c*) are doubtless the dwarf cells seen in dried and stained preparations. Curiously enough, these fragments tend again to assume the biconcavity characteristic of normal cells, as a drop of fat breaks into smaller but similar drops.

(*d*) *Oval Shape.*—In a great many cases of pernicious anæmia and some other forms of anæmia there is a marked tendency to oval shapes in corpuscles not otherwise considerably deformed. Even in normal blood I think there are a small number of oval forms, and in anæmia this number may be greatly increased till, as in Fig. 25, we get all the cells elongated. The same appearance can be produced by roughness in spreading the blood, but in such case the deformed corpuscles all point one way.

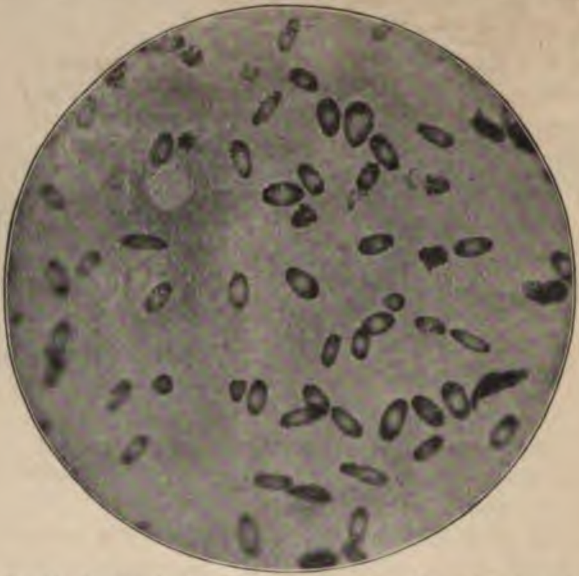

FIG. 25.—Elongated or Oval Corpuscles in a Case of Pernicious Anæmia.

(*e*) *Changes in Staining Properties.*—Normal red corpuscles have affinity chiefly for acid stains. Influences like those which lead to the alterations in shape and size above described may alter the staining properties of the cell as well, so that it takes up two or three colors (according to the number present in the stain), either diffusely or irregularly, some parts of the cell taking color differently from others. In lead poisoning, for example, minute

PLATE A.

FIG. 1.—*m*, *m*, etc., Megaloblasts, some with polychromatophilic protoplasm, some with degenerating nuclei (karyolysis).

mi, *mi*, Microblasts.
n, Normoblast.
f, "Free" nucleus.
b, Blue cell (*i.e.*, basophilic erythrocyte) with nuclear remnant.
r, Ring body in red-stippled erythrocyte.
s, Blue-stippled erythrocyte.

FIG. 2.—*m*, *m*, etc., Myelocytes.

p, *p*, etc., Polynuclears.
t, *t*, Transitional neutrophiles.
l, Lymphocyte.
n, *n*, Normoblasts.
me, Eosinophilic myelocyte.
b, Mast cell.
e, Eosinophile.

EXAMINATION OF THE BLOOD. PLATE A.

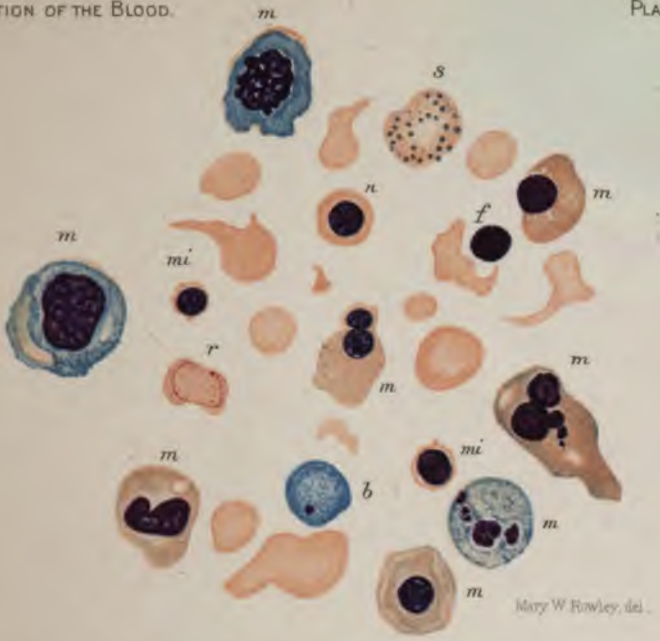

Fig. 1. RED CELLS, – nucleated deformed or abnormally stained.
(Wright's modification of Leishman's stain.)

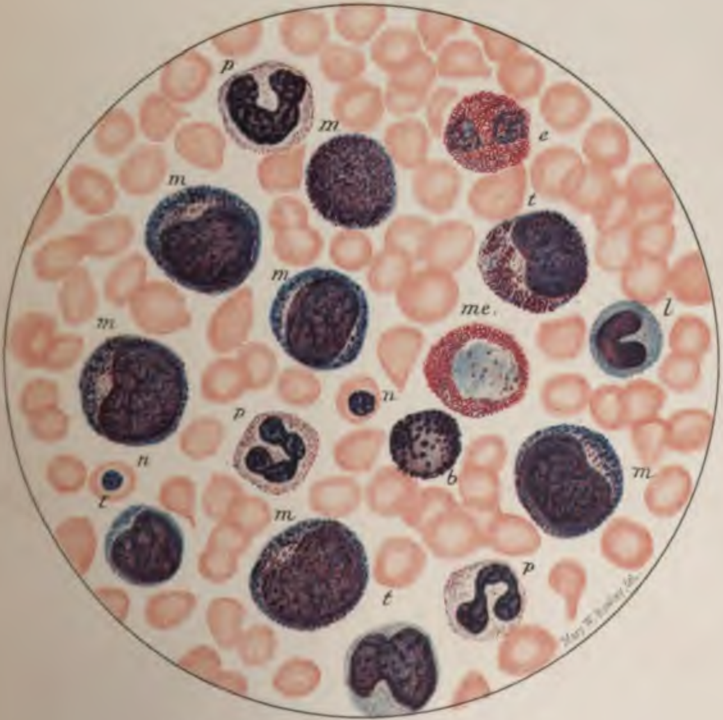

Fig. 2. MYELOGENOUS LEUCAEMIA
(Wright's modification of Leishman's stain.)

Geo. H. Walker & Co. Lith.

bits of the red cells become basophilic, so that the cell presents, with appropriate staining, a stippled look. The same change occurs in pernicious anæmia and occasionally in other varieties of anæmia. This has been termed a "*polychromatophilic*" or degenerative change. Some observers have supposed it to be rather of the nature of *regeneration*, believing that the cells take color in this unorthodox way because they are half-developed.[1]

(*f*) In many secondary anæmias, especially in those associated with inflammations, the average diameter of the cells is lessened, and the rouleaux are not formed.[2]

(*g*) Cells may lose their hæmoglobin altogether, leaving only the shell of the corpuscle behind (see Fig. 24, *d*).

All these necrobiotic changes are characteristic of the severer grades of secondary anæmia, such as occur in cancerous cachexia, phthisis, nephritis, etc.

III. *Third Stage.*—Here the *number* as well as the *quality* of the red cells begins to suffer. So far I have mentioned only the qualitative changes in secondary anæmia and have purposely made these changes more prominent than the actual diminution in the count of red cells, because it is only comparatively rarely and in very marked cases that the diminution in corpuscles is considerable. The blood characteristic of most cases of secondary anæmia is one in which the number of red cells is approximately normal.

The important exceptions to this rule are: 1. The anæmias of infancy and early childhood. 2. Large hemorrhages (soon after their occurrence). 3. Malaria. 4. Acute septicæmia.

The direct and rapid destruction of the corpuscles by the malarial organism or hemorrhage account for this. Of sepsis and the anæmias of infancy I shall speak later.

IV. *Fourth Stage.*—The blood of secondary anæmia shows often evidence not only of degeneration and destruction of the cells but also of regenerative changes. I have already described two regenerative changes—basophilic stippling and diffuse polychromasia; a third is the presence of

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[1] A heated controversy has sprung up regarding this point and a considerable mass of literature relating to it has accumulated. Without trying to present and criticise the evidence I shall content myself with stating that all the changes in staining reaction, just described, seem to me best explained as evidence of *regeneration*.

[2] But in the severest forms of anæmia the diameters are apt to be increased.

Nucleated Red Cells.

These are usually divided into three groups

(*a*) Normablasts.
(*b*) Megaloblasts.
(*c*) Microblasts.

Normoblasts.

(*a*) The first are normally present in moderate number in the bone marrow of healthy persons, and in great numbers in the marrow after hemorrhage. They are generally considered to be a younger stage in the life of the corpuscle than the non-nucleated forms seen in the circulating blood. Hence the appearance in the peripheral circulation of this form of nucleated cell is considered to mean that, in the comparatively plentiful reproduction of red cells called forth in the marrow by the anæmia, a certain number of red cells leave the nursery (the marrow) before they are grown up and circulate for a time in their immature state. A normoblast, then, represents an immature red corpuscle (see Plate IV. and Plate A.)

In size and color it is like an ordinary red cell except that we find, usually somewhat to one side of it, a round nucleus about one-half the diameter of the whole cell. With Ehrlich's or Wright's stain this nucleus stains very deep blue, nearly black, and is sharply outlined against the pale yellow of the cell body around it.

The cell often looks as if it were pushing its nucleus out, *i.e.*, in many instances we see the nucleus projecting over the edge of the corpuscle, or half out of it, and occasionally we find it lying beside the corpuscle from which it has just emerged; but this appearance is probably an artifact and not, as Ehrlich thought, the regular way of disposing of the normoblast nucleus.

Very frequently the nucleus has towards the centre a light spot, sometimes so brilliant that it looks like the reflection of light from the surface of a drop of ink or any dark liquid, what artists call the "high light." Occasionally there are several of these light spots in a nucleus, or it may be all light blue-gray except a dark blue rim. This is the commonest type of normoblast. But now and then we meet with one when the nucleus is more or less separated into two or more pieces. These pieces are usually connected by pale-staining "bridges," perhaps radiating from a centre so that

PLATE IV.

(1) *m, m, m, m—Young megaloblasts.*

(2) *D, D, D, D*; the *upper two* are probably *old normoblasts* with degenerating nuclei, and the lower two old megaloblasts with nuclei in a similar condition.

(3) *o, o, o, o,* etc.—The two cells in the lower right-hand corner are probably *old megaloblasts* whose nuclei are nearly absorbed. The three cells immediately to the left of these are probably *young normoblasts*—the lowest one being the youngest. The other four cells marked "*o, o, o, o*" (those to the extreme left) are probably *middle-aged megaloblasts.* The two labelled "Normoblasts" are really *old normoblasts.* The appearance of extrusion of the nucleus on one of them is probably an artifact. The large cell on the extreme upper right-hand corner is probably a megaloblast with a "pyknotic" or œdematous (degenerating) nucleus.

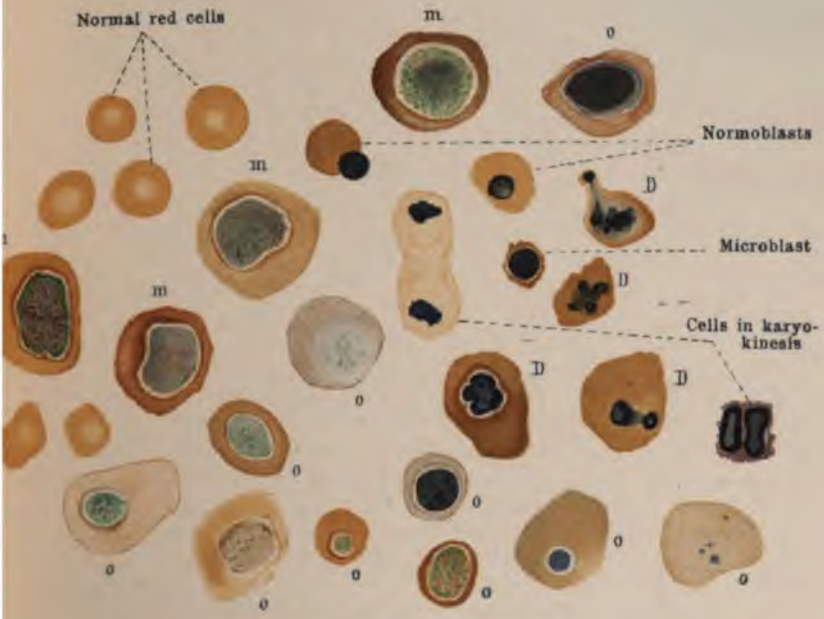
(4) In the young or "typical" megaloblasts (*m, m, m, m*) note the white line around the nucleus, the variations in its tint, and, in two of them, the discolorations of the protoplasm (polychromatophilia), especially near the nucleus. The lower of the two cells in karyokinesis shows the best.

(5) In the *microblast* note the ragged edge of the protoplasm.

(6) In the lower portion of the plate ("*cells deformed in size or shape*") an actual field from a case of pernicious anæmia was copied. *Macrocytes* (or large cells), *microcytes* (or small cells), and misshapen cells or *poikilocytes* are shown.

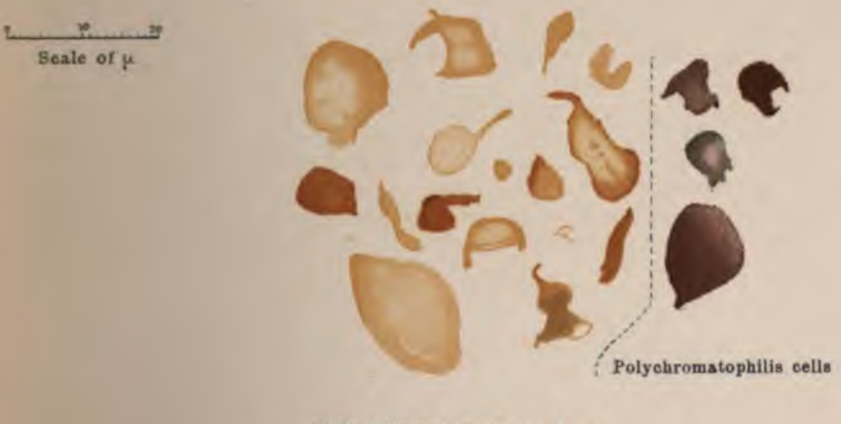
(7) The "*polychromatophilic cells*" in the lower right-hand corner were stained with the same mixture as those to the left of them, but have taken up other colors besides the orange G, which alone is taken up by normal red cells.

PLATE IV.



Varieties of Nucleated Red Cells.

m. m. m. m. = Typical megaloblasts. D. D. D. D. = Cells with dividing nuclei.
o. o. o. o. o. o. o. = Other (unnamed) varieties of nucleated red corpuscles.



Cells deformed in size or shape.

Cabot fec.
Lith. Anst. v. E. A. Funke, Leipzig.

the nucleus is "rosette-shaped," or it may take any one of a large number of different shapes. The parts of the nucleus which are nearest the periphery of the cell usually stain more deeply than the "bridges" which join them.

Sometimes the nucleus breaks apart completely, and we find two or more separate unconnected nuclei within the single cell.[1] Or one of the pieces may be outside the cell and the others inside.

Rarest of all is the appearance of true mitosis in the nucleus of a normoblast.

Megaloblasts.

(*b*) The typical megaloblast, as usually described, is so unlike the normoblast that we should not naturally think of them as near relations.

It does not occur anywhere in the healthy adult body, not even in the bone marrow. In the early fœtal marrow and in the marrow and circulating blood of grave forms of anæmia it is to be found, usually in company with a certain number of normoblasts.

The *typical megaloblast* is an abnormally large cell (11 to 20 μ in diameter), frequently showing abnormal staining (polychromatophilia) in its protoplasm, which is, therefore, brownish or purplish with the Ehrlich's stain, gray or yellowish with Wright's. Its nucleus is very large, filling most of the cell, and contrasts with the normoblast nucleus not only by its greater size, but by the pale, even stain which it takes up. The commonest color of the nucleus with the Ehrlich-Biondi stain is pale green or robin's-egg color; with Wright's stain some shade of blue (see Plates IV. B, E, and F).

Cracks and "flaws" are sometimes to be seen in the protoplasm, giving evidence, as its purplish stain does, of the necrobiotic changes described by Maragliano.

The outline of the whole may be quite circular: oftener it is oval or somewhat irregular, but rarely much deformed.

Microblasts

(*c*) Microblasts, which are rarer than either of the varieties just described, consist of a nucleus like that of a normoblast or smaller, and contained in a cell body *smaller* than the normal red corpuscle.

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[1] Apparently the nucleus is absorbed or degenerates (see Israel and Pappenheim. Virchow's Archiv, vol. cxliii.).

In the writer's experience the cell body is usually reduced to a few shreds of discolored protoplasm changing about the nucleus (see Plate IV.). Their clinical significance is generally supposed to be that of megaloblasts.

"*Atypical Forms.*"

We may find in a given specimen of blood *only* typical normoblasts, microblasts, or megaloblasts, and accordingly can easily reckon up the number of each kind and see which type of blood formation predominates. But sometimes there are cells present about the classification of which we cannot come to a decision, and I have occasionally seen a specimen of blood containing a large number of nucleated red cells *no one of which* could strictly be classed *either* as a "normoblast," a "megaloblast," or a "microblast," as these are defined above. The researches of Pappenheim have thrown much light on this difficulty. While insisting with Ehrlich that the megaloblast and the normoblast represent respectively the early fœtal and the post-uterine types of blood formation, and that there are no real "transitions" from the one to the other, he yet recognizes that the two varieties are not *absolutely* to be differentiated by any of the ordinarily accepted criteria such as size, color of nucleus, etc. *Most* "megaloblasts," he admits, are larger than *most* normoblasts, but there are occasional giant normoblasts and dwarf megaloblasts which by size alone are indistinguishable. The large, pale, delicately netted nucleus of the "megaloblasts" is simply a *young* nucleus. All young nuclei are relatively large and pale, while the small dark nucleus of the normoblast is simply an *old* or degenerating nucleus. The *real* criteria of the two varieties, according to Pappenheim, is not the size or color of nucleus nor of the whole cell, but the structure of the nuclear network. This is a point difficult to make out by ordinary staining methods and not easily appreciated. Luckily for us, most "megaloblasts" *are* larger than most "normoblasts"; and further, most of them, as seen in the blood, are *young* (*i.e.*, have large pale nuclei with delicate chromatin network), while most "normoblasts" are *old*, as shown by their small, dark, coarse-skeined nucleus, so that in the majority of cases Ehrlich's criteria for the two varieties are sufficiently correct for diagnostic purposes. Pappenheim of course wishes to abandon the terms "megaloblast" and "normoblast" altogether, but since size still remains the most easily recognized

PLATE F.

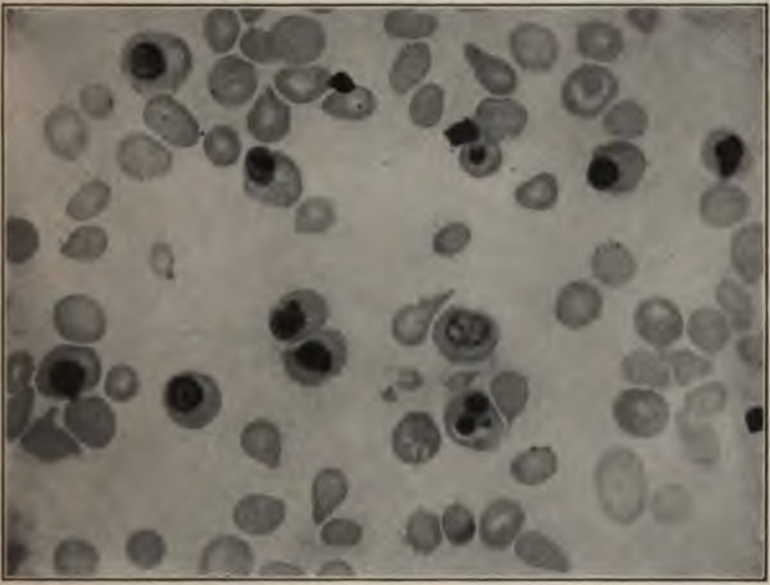

FIG. 1.—Erythroblasts in Pernicious Anæmia.
(From a slide kindly loaned by Dr. A. L. Knight, of Cincinnati, and showing an extraordinary abundance of erythroblasts.)

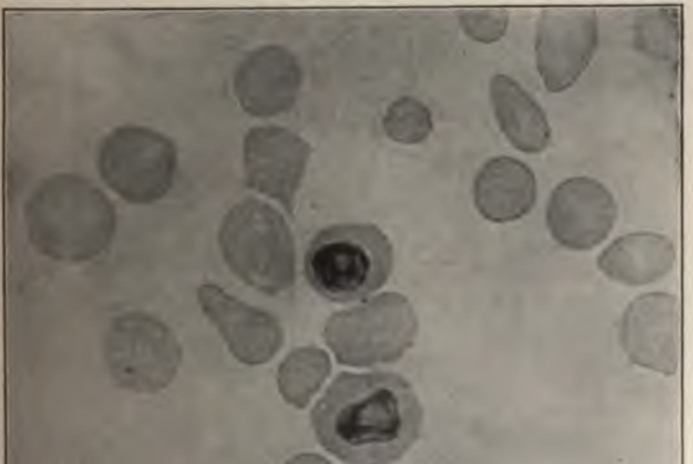

FIG. 2.—Megaloblasts in Pernicious Anæmia.
(Part of the same slide shown in Fig. 1 above more highly magnified.)

criterion of "megaloblasts" and "normoblasts" I shall continue to use the terms. On the chances, then, *any nucleated red cell over 10 μ diameter should be classed as a megaloblast whatever the appearance of its nucleus*, and *any nucleated red cell under 10 μ diameter is probably a normoblast* whatever the appearance of its nucleus. *Microblasts* simply represent degenerating forms (usually normoblasts) whose protoplasm is falling away. [These points will be made clearer by reference to Plate IV. and the remarks intended to explain it.]

In most cases of severe secondary anæmia we find a few normoblasts. In very severe forms, whatever the cause, we may or may not find an occasional megaloblast. But these are usually rarer than the normoblasts, even in the severest types of secondary anæmia. The commonest exceptions to this rule are the anæmias due to hæmolysis, or to intestinal parasites, in which, though secondary and curable, the megaloblasts in some cases predominate over the normoblasts.

Summing up the changes characteristic of secondary anæmia, which includes almost all the important pathological appearances occurring in red cells, we have:

I.	(*a*) Lack of hæmoglobin. (*b*) Lowered specific gravity.	Characteristic of mild cases.
II.	The above and necrobiotic changes of Maragliano.	Characteristic of moderate cases.
III.	(*a*) Lack of red cells. (*b*) Presence of normoblasts and the above (I. and II.).	Characteristic of severe cases.
IV.	Megaloblasts and the above (I., II., and III.).	Characteristic of very severe cases.

The changes in the white cells will be discussed in the next chapter.

Among the commonest causes of secondary anæmia are: I. Infective and febrile diseases, acute or chronic. II. Malignant disease. III. Chronic suppurations, nephritis, chronic dysentery, cirrhosis of the liver. IV. Bad hygiene, pregnancy, and lactation. V. Intestinal parasites. VI. Poisons (lead, arsenic, etc.).

To discuss the way in which each of these influences acts in producing anæmia is tempting, but falls outside the plan of this book.

The following are good examples of the condition of the blood:

SECONDARY ANÆMIA.

No.	Age.	Red cells.	White cells.	Hæmoglobin.	Remarks.
1	23	1,656,000	2,300	18	Post malarial.
		2,048,000	2,600	24	Seven days' treatment.
		1,808,000	3,200	30	Fourteen days' treatment.
		1,568,000	1,300	58	Twenty-four days' treatment.
		4,248,000	2,300	60	Thirty-four days' treatment.
2	22	1,540,000	2,200	....	Malaria and dysentery.
3	23	1,984,000	6,700	....	" " "
4	21	1,352,000	3,300	....	" " "
5	24	1,248,000	6,000	....	" " "
6	23	1,931,000	8,600	35	Æstivo-autumnal malaria.
					Polynuclears, 73; lymphocytes, 24; eosinophiles, 3; megaloblasts = 1; normoblasts, 4.
7	35	3,070,000	2,100	35	Tertian malaria. Boston.
8	29	1,228,000	25,100	9	Tubal pregnancy, hemorrhage. Polynuclears, 92; lymphocytes, 7; eosinophiles, 1; normoblasts = 6; megaloblasts = 2.
9	50	1,960,000	13,400	22	Fibroid bleeding. Polynuclears, 85; lymphocytes, 14; eosinophiles, 1.
10	64	1,824,000	4,800	25	Hæmaturia.
11	25	1,448,000	3,600	10	Portal thrombosis, profuse hæmatemesis. Polynuclears, 79; lymphocytes, 19; eosinophiles, 2; normoblasts = 3; megaloblasts = 1.
		906,000	......	6	Ten days later. Death next day. Autopsy.
12	39	3,200,000	20,000	52	Hepatic cirrhosis. Hæmoptysis yesterday.
13	46	2,992,000	13,800	20	Metrorrhagia.
14	31	2,500,000	7,500	30	Chronic diffuse nephritis.
15	40	2,040,000	9,600	10	Chronic dysentery. Polynuclears, 66.3; myelocytes, 1.4; normoblasts = 8; megaloblasts = 5. (Four hundred cells counted.)
16	53	4,030,000	12,700	23	Mitral stenosis. Skin lemon-yellow. Autopsy. Polynuclears, 82; lymphocytes, 18; eosinophiles, 0; megaloblasts = 4; normoblasts = 22. (Four hundred cells counted.)
17	33	2,999,000	9,200	35	Chronic arthritis with ankylosis.
18	39	3,584,000	12,000	45	Alcoholic neuritis.
19	30	3,496,000	11,000	25	Chronic gastric catarrh.
20	42	3,020,000	11,600	50	Tertiary syphilis.
21	25	3,712,000	10,200	40	Ovarian cyst.
22	11	4,240,000	11,600	45	Friedreich's ataxia.
23	9	4,270,000	9,200	35	Cervical Pott's.
24	58	2,744,000	4,000	60	Autopsy. No cause found.
25	59	2,444,000	4,700	38	Polynuclear, 73; lymphocytes, 25; eosinophiles, 2; normoblasts = 2; megaloblasts = 0.
26	43	1,468,000	8,700	12	Polynuclears, 71; lymphocytes, 27.8; eosinophiles, 1; myelocytes, 2; normoblasts = 7; megaloblasts = 1. Autopsy, fibroma of jejunum (ulcerative colitis).
27	53	1,472,000	12,400	20	Duodenal ulcer. Polynuclears, 75; lymphocytes, 23.6; eosinophiles, 1.2; myelocytes, 2; normoblasts = 1.
		1,876,000	......	19	Seventh day.
		2,148,000	......	17	Fourteenth day.
		2,440,000	......	21	Twenty-first day.
		3,196,000	......	23	Twenty-eighth day.
		2,774,000	6,600	28	Thirty-fifth day.
				23	Forty-third day. Polynuclears, 72.8; lymphocytes, 25; eosinophiles, 2; mast cells, 2; normoblasts = 1.
		2,820,000	......	30	Fiftieth day.
		3,440,000	......	43	Fifty-seventh day.
		3,832,000	......	46	Sixty-fourth day.
		3,885,000	......	48	One hundred and second day.

2 HYDRÆMIA.

(*a*) Seen from the opposite point of view almost all cases of anæmia are hydræmic. That is, if the total volume of blood is to remain approximately constant (as it appears to do), any loss of

PLATE E.

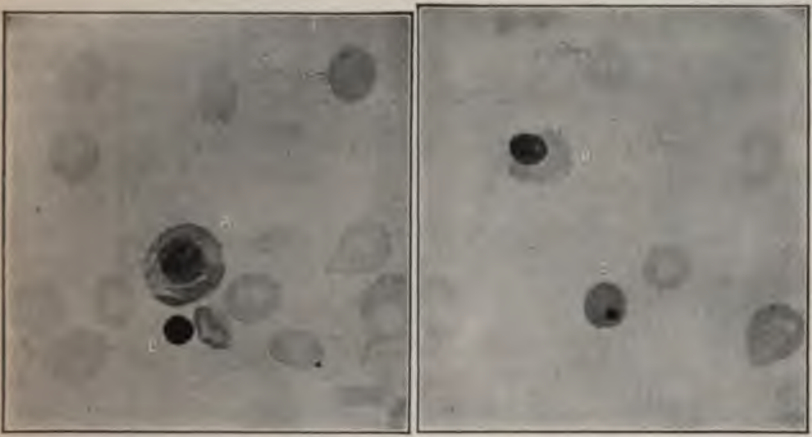

FIG. 1.—Erythroblasts in Pernicious Anæmia. *A*, Megaloblast; *B*, "free" nucleus; *C*, cell containing a small remnant of a nucleus which is nearly absorbed; *D*, nucleus apparently "loose" in a cell.

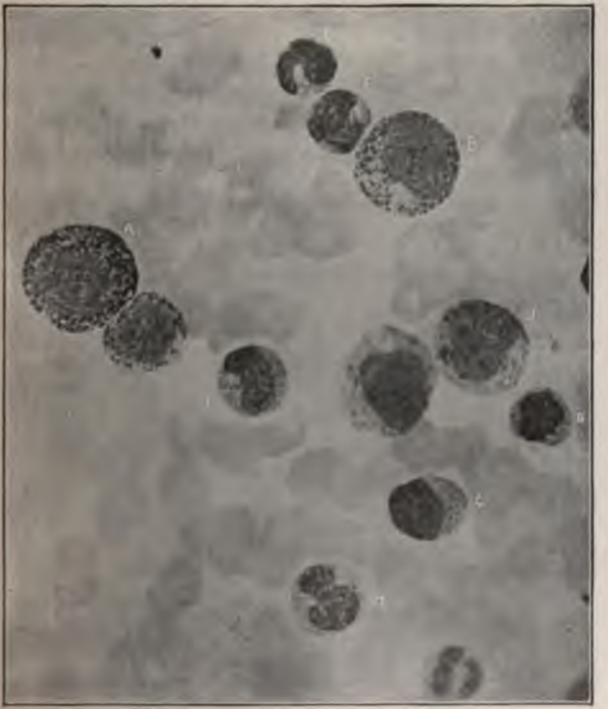

FIG. 2.—Myelogenous Leukæmia. *A*, *B*, *C*, Typical myelocytes; *D*, *E*, *F*, *G*, and *H*, cells intermediate between myelocytes and polynuclear neutrophiles; *I*, *J*, cells possessing characteristics in part of large lymphocytes, in part of myelocytes.

solids (corpuscle substance) must be made up by water taken in from the tissues. Hence any anæmic person's blood is thin, watery, or hydræmic. Women's blood is somewhat more hydræmic than men's, because less rich in cells. Ordinary chlorosis and secondary anæmia show no more water than normal in the serum, but the cells are probably somewhat waterlogged.

(*b*) In many conditions of dropsy, whether from heart or kidney, we may have more water than normal, both in the plasma and in the corpuscles themselves, which are capable of taking up considerably more than their normal amount of water.

(*c*) Any temporary dilution of the blood under the conditions mentioned above (ingestion of liquid, lowered blood pressure, etc.), is from one point of view a hydræmic condition.

No special clinical significance attaches to it other than that of anæmia, whose correlative it is.

(*d*) The investigations of Haldane and Smith seem to show that the total *volume* of plasma is greatly increased in certain types of anæmia, although its specific gravity remains normal. This is one type of hydræmia (see page 6).

CHAPTER VIII.

LEUCOCYTOSIS—LYMPHOCYTOSIS—EOSINOPHILIA—MYELOCYTES.

Much confusion has been caused in the past by the failure to see in leukæmic blood anything more than an extreme and permanent form of leucocytosis, while leucocytosis was thought of as a mild and temporary leukæmia.

We know now that they are quite different phenomena, differing not in the number, but in the *kind* of cells present in the increased numbers.

Definition.

There are many difficulties in defining leucocytosis. To my mind the term is best used to mean: *An increase in the number of leucocytes in the peripheral blood over the number normal in the individual case, this increase never involving a diminution in the polymorphonuclear varieties, but generally a marked absolute and relative gain over the number previously present.*

(*a*) I say "in the peripheral blood" because most observers now hold that leucocytosis is not always a real increase in the total number of leucocytes in the body, but is often the result of chemotaxis or thermotaxis, the cells being drawn or attracted to the periphery and out of the internal organs. At any rate, in the blood drop which we draw (whether also in the internal organs or not), the leucocytes are present in increased numbers per cubic millimetre. The studies of Muir, Ehrlich, and others have made it clear that there are two types of leucocytosis. (1) The first includes only leucocytoses of sudden appearance and short duration such as those produced by cold baths. Here there is no time for the production of new cells and the increase of white corpuscles in the peripheral blood corresponds in all probability to a decrease in the number ordinarily hoarded in the pulmonary capillaries and elsewhere, the total number of leucocytes in the body remaining approximately the same. (2) When leucocytosis lasts for months, as is often the case in long-standing suppurations and malignant neoplasms, there is no doubt that leucocytes are formed and turned into the circulation more rapidly than under normal conditions. The total number of leucocytes in the body is then greatly increased. In such cases the marrow is found to be hyperplastic whether the leucocytosis is due to bacterial toxins (Ribbert) or to long-continued experimental injections of albumoses (Taylor). Chronic leucocytosis, then, is a function of the marrow.

(*b*) In persons not usually to be considered sick, but simply somewhat wizened or ill-nourished, the normal count of white cells may be as low as three thousand per cubic millimetre. For such an individual ten thousand cells per cubic millimetre would be a decidedly pathological condition. On the other hand, there are persons, usually those of notable vigor and good nutrition, whose white cells rarely fall below ten thousand.

Obviously we must take account of these differences both in our definition and in our practice if we are to reason correctly from the data of blood examination.

(*c*) Further we must lay stress upon the varieties of leucocytes whose increase constitutes leucocytosis in distinction from either variety of leukæmia (myeloid or lymphatic).

For instance, given a count of eighty thousand leucocytes per cubic millimetre, we cannot tell without knowing the varieties of cells present whether the case is a genuine leukæmia or merely a leucocytosis symptomatic of pneumonia, suppuration, malignant disease, or other conditions.

(*d*) Lastly, in order to be sure that the polymorphonuclear cells are not decreased, we must know approximately what the normal percentage *for that individual* is. The normal percentage of these cells in infancy is from twenty-eight to forty per cent. In adults it is much higher, but varies like the total count, according to conditions of nutrition, etc. Thus the normal for adults is usually set at from sixty to seventy per cent, and if we include the obviously ill-nourished, but not actually sick, and also those in blooming health, we shall have to widen our normal limits considerably. From fifty to seventy-five per cent are within normal limits according to the above conception. But obviously we can make no absolute judgment by a standard so vague. It is much better, I think, to consider each individual as his own standard within these limits, his count of polymorphonuclear cells being a fair measure of the soundness and vigor of his metabolism Thus, in an obviously debilitated individual, we should consider seventy-two per cent of these cells very high, while in a vigorous athlete it might not be so. In typical leucocytoses of the inflammatory type the percentage of polynuclear cells often rises above eighty per cent, sometimes much higher; but very rarely as high as in the case of suppurative meningitis mentioned by Stengel—*99.5* per cent.

It is the endeavor to include all these limiting conditions that has made my definition so long and involved.

Whether or not differences of race make any difference in the normal count of white cells I cannot say, but certainly the average of a group of college athletes would be higher than that of some country towns in New England, where everybody is more or less under-nourished; and if one is to practise among all sorts and conditions of men, I think he cannot but expect to find people's leucocytes vary all the way *from 5,000 to 10,500 per cubic millimetre*, without there being more than malnutrition to account for the lower figures.

We may divide leucocytoses for convenience's sake into: 1. Physiological leucocytoses. 2. Pathological leucocytoses.

PHYSIOLOGICAL LEUCOCYTOSES.

1. Leucocytosis of the new-born
2. Leucocytosis of digestion.
3. Leucocytosis of pregnancy.
4. Leucocytosis post partum.
5. Leucocytosis after violent exercise, massage, and cold baths.
6. Leucocytosis of the moribund state.

The Leucocytosis as Affected by Digestion and the Time of Day.

(*a*) Total abstinence from food lowers the leucocyte count. In the blood of the professional faster Succi, the number sank within his first week's fast to 861 per cubic millimetre. After the first week it rose to 1,530, and remained there throughout his thirty days' abstinence (Luciani).[1] The polymorphonuclear cells and eosinophiles are said by Tauszk to be increased in chronic starvation.

Von Limbeck counted the blood of a melancholic patient who had fasted a week, and found 2,800 white cells per cubic millimetre. These facts support the idea that the number of leucocytes depends

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[1] "Das Hungern," German translation by O. Fränkel. Hamburg, 1890.

(within certain limits) on the individual's assimilation of food. In cancer of the gullet we find similar low figures.

(*b*) After a midday meal rich in proteids the leucocyte count rises about thirty-three per cent in many sound persons. Ten thousand cells may perhaps be considered the average, three to four hours after a proteid meal; but if the count before a meal is only 4,000 or 5,000, digestion will perhaps not raise it above 7,000, while vigorous adults may show 13,000. Examples of the midday meal leucocytosis in diseases other than gastric are seen in the following table:

Case.	Diagnosis.	Count before food.	Count after food.
1	Cirrhosis	10,000	18,900
2	Pneumonia	10,400	21,700
3	Neurasthenia	7,500	13,500
4	Adhesions around gall-bladder.	5,450	8,650

Occasionally we see sound persons with little or no leucocytosis of this type.

Any disease of the gastro-intestinal tract, whether functional or organic, may prevent the appearance of the midday leucocytosis (see later under Diseases of the Stomach, page 436). In anæmic and debilitated conditions it is frequently absent.

Food may call forth a considerable leucocytosis when it is a *novelty* in the stomach. Patients with gastric ulcer who have been fed exclusively by rectum for some weeks may show a marked leucocytosis after their first meal.

Japha (*Jahrbuch für Kinderh.*, N.F., vol. lii., p. 242), who has recently gone over the subject afresh, finds that in infancy there is no regular digestion leucocytosis, and that in adults a leucocytosis is frequently absent after breakfast and supper, appearing only or chiefly after the midday meal, even though the other meals be rich in proteids.

Further, Japha proved that *even in fasting persons* an increase of leucocytes occurs about midday, and hence he believes that the so-called digestion leucocytosis represents, in fact, only or chiefly a *periodic daily variation* like that of blood pressure or respiration.

Burian and Schur[1] found an increase of the polymorphonuclear varieties in those cases in which an increase of the total count took place at all and Japha's figures support this. Rieder reports a lymphocytosis. It is probable that both lymphocytes and neutrophiles are increased, while eosinophiles are not markedly affected.

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[1] Wien. klin. Woch., February 11th, 1897.

In view of these facts, it seems to me that the so-called digestion leucocytosis probably represents, as Japha suggests, a periodic daily variation—at any rate, in part. In routine blood examinations allowance should be made for it, but I do not see that it has any diagnostic value.

Leucocytosis of the New-Born

The following table is compiled from the best authorities on the subject (Schiff, Gundobin, Bayer, Hayem, Carstanjen, Warfield, and others):

Age.	Red cells.	Leucocytes.
At birth	5,900,000	17,000 to 34,000
End of first day	7,000,000 to 8,800,000	24,000
" second day	Generally increased.	18,000
" fourth day	6,000,000	
" seventh day	5,000,000	
Tenth day	....	10,000 to 14,000
Twelfth to eighteenth day	....	12,000
Sixth month	....	12,000
Sixth year and upward	....	7,500

The counts just after birth are higher than at any other time of normal life. Children born after a long hard labor or delivered instrumentally after long labor show the highest counts.

A fuller discussion of the subject will be found in the chapter on the blood in infancy.

The Leucocytes in Pregnancy

On the authority of older writers it has been generally stated up to the present time in books on the blood (including this one) that there is a moderate leucocytosis in primiparæ and in fifty per cent of multiparæ during the later months of pregnancy. But the more recent and thorough investigations on this subject have not confirmed the earlier statements.

Greco (*Archiv. de Ostet. e Ginecol.*, December, 1899) studied thirty-six cases and found no leucocytosis and no abnormality in the differential count.

Zangemeister (*Deut. med. Woch.*, July 31st, 1902) compared the blood of fifty-seven pregnant women with that of forty-seven healthy non-pregnant women and found no considerable difference between the counts in the two series.

Ascoli and Esdra (cited from Hahl: *Arch. f. Gynäkol.*, 1902, p. 491) investigated seventeen cases at various periods in the pregnancy and found no genuine leucocytosis and no progressive increase.

Hahl (*loc. cit.*) found practically no increase before the beginning of labor.

Leucocytosis After Parturition.

Hibbard and White (*Jour. Exp. Med.*, November, 1898) studied fifty-five cases, thirty-three of which were in primiparæ. Twenty-four hours before labor eighty-four per cent of the primiparæ showed leucocytosis (*i.e.*, over 10,000 per cubic millimetre), the average being 15,000, while in seventy-five per cent of multiparæ there was some increase (11,700 average).

After delivery there was a decided fall in the leucocyte count, which was normal about the fourth day with a slight secondary rise about the fifth to the seventh day post partum. After this the leucocytes gradually fell to normal. The leucocytosis was more marked in the younger women and in primiparæ.

During labor itself the counts rose from an average of 12,200 to an average of 17,600 in primiparæ, and from 9,600 to 12,200 in multiparæ Mastitis produced a rapid rise of leucocytes.

In all cases the increase was made up by the polynuclear cells alone, while eosinophiles were usually scanty or absent.

Hahl (*loc. cit.*) studied thirty-six cases (twenty-one primiparæ fifteen multiparæ) and concludes: "1. During the last day of pregnancy the leucocytes are somewhat increased. The beginning of labor pains produces a further and rapid increase made up wholly of the polynuclear cells. 2. In the course of the first week after delivery the leucocytes return to normal."

Zangemeister (*loc. cit.*) confirms the above, and adds that in especially difficult or painful labors the leucocytes are proportionally increased (*e.g.*, to 30,000 or more). In the puerperium very high counts were found only when there was marked absorption of decomposed lochia. He believes that no diagnostic or prognostic value can be placed upon leucocyte counts in the puerperium.

The articles of Henderson (*British Journ. of Obst. and Gyn.*, 1902, p. 168) and of Pray (*American Gyn.*, October, 1902) confirm in essentials these findings.

The Leucocytosis of Violent Exercise.

Larrabee, Tileston, and Emerson[1] have recently studied the blood of eleven men before and after a twenty-five-mile road race on foot. Their results are summarized in the table on page 95.

The most striking point is the resemblance of the blood to that found in leucocytoses of the inflammatory or toxic (distinctly pathological) type. Even the abnormal forms of leucocytes—myelocytes, transitional neutrophiles, and "stimulation forms"—were present in some cases, while eosinophiles were reduced or absent.

Cold Baths and Massage.

Thayer studied twenty cases of typhoid and found an average of 7,724 white cells before and 13,170 after a Brand bath (*Johns Hopkins Medical Bulletin*, April, 1893). The increase took place equally in all varieties. Winternitz (Imperio-Royal Medical Society, Vienna, February, 1893) came to a similar conclusion and found also that prolonged cold bathing decreased the number of white cells (dry cold does the same). A patient was recently brought to the Massachusetts Hospital who had fallen through a hole in the ice and been some minutes in the icy water. His temperature was 91.8° by the rectum. Blood count showed 17,500 leucocytes per cubic millimetre. Next day he was perfectly well.

On the contrary, short hot baths decrease and prolonged ones increase the number of leucocytes. Local warm baths have a similar effect, raising the count of leucocytes in the blood of the immersed arm if cold and short, and lowering it if hot and short, while prolonged immersion has an opposite effect. In the other arm the counts go up when those of the immersed arm go down, and *vice versa* (Rovighi).[2] Mitchell[3] found that the leucocytes showed distinct increase (as well as the red cells and hæmoglobin) after one hour's general massage.

These forms of leucocytosis are usually explained by changes in blood pressure, and vasomotor changes affecting the calibre of the peripheral vessels and consequently their contents. Becker[4] found

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[1] Boston Med. and Surg. Journal, February 19th, 1903.

[2] Arch. Ital. d. Clin. Med., xxxii., 3, 1893.

[3] American Journal of the Medical Sciences, May, 1894.

[4] Deutch. Arch. f. klin. Med., 1901, vol. lxx.

NAME.	Year.	BEFORE RACE.								AFTER RACE.								REMARKS.
		* Reds.	Total whites.	Polymorphonuclear neutrophiles.	Small mononuclears.	Large mononuclears and transitionals.	Eosinophiles.	Mast cells.	Myelocytes.	Reds.	Total whites.	Polymorphonuclear neutrophiles.	Small mononuclears.	Large mononuclears and transitionals.	Eosinophiles.	Mast cells.	Myelocytes.	
J. L....	1901	......	*5,800	63.2% 3,666	26.8% 1,554	8.2% 476	1.8% 104	...	0	......	16,209	90.3% 14,629	4.5% 729	4.4% 713	0	...	0.8% 130	Many cells intermediate between polymorphonuclears and myelocytes.
H—ks..	"	......	4,800	72.8% 3,494	18.2% 874	8.2% 394	0.8% 38	...	0	......	14,400	88.5% 12,744	7.0% 1,008	4.4% 634	0	...	0.1% 14	
McA...	"	......	3,700	72.0% 2,664	14.6% 540	10.6% 392	2.6% 96	...	0.2% 7	......	20,800	83.8% 17,430	7.8% 1,622	8.2% 1,706	0.2% 42	...	0	
P......	"	......	*8,200	74.0% 6,068	18.4% 1,509	5.6% 459	2.0% 164	...	0	......	22,200	86.1% 19,114	6.6% 1,465	7.1% 1,576	0	...	0.2% 44	Few cells intermediate between polymorphonuclears and myelocytes.
J. L....	1902	4,450,400	4,333	57.5% 2,491	29.4% 1,274	12.2% 529	0.8% 35	0.1% 4	0	4,340,800	14,200	86.4% 12,269	6.5% 923	6.8% 965	0	0	0.3% 43	Pale, much exhausted.
C......	"	(Apr. 17) 4,808,000	5,200	66.6% 3,464	19.7% 1,024	11.4% 593	1.7% 88	0.6% 31	0	6,074,400	20,400	88.5% 18,055	2.2% 449	9.1% 1,856	0.1% 20	0.1% 20	0	Good condition at finish.
H—n...	"	(Apr. 17) 4,872,000	5,700	70.1% 3,996	18.5% 1,055	9.9% 564	1.2% 68	0.3% 17	0	Not taken	18,200	83.7% 15,234	6.9% 1,256	9.0% 1,638	0.2% 36	0.1% 18	0.1% 18	Ran but 14 miles. Examined 3 hours after finish.
P......	"	(Apr. 17) 5,392,000	8,000	53.9% 4,312	28.2% 2,256	13.4% 1,072	3.7% 296	0.8% 64	0	5,418,600	27,500	79.6% 21,890	6.7% 1,843	13.1% 3,603	0.3% 82	0.1% 27	0.2% 55	
H—ks..	"	5,516,000	6,000	71.7% 4,302	19.6% 1,176	7.6% 456	0.8% 48	0.3% 18	0	6,168,000	22,600	87.4% 19,752	4.2% 949	8.2% 1,853	0.1% 23	0	0.1% 23	Cyanosis. Ran but 15 miles. Examined 1½ hours after finish.
F......	"	4,826,000	7,600	....	....	....	...	...	...	......	22,600	.....	....	....	...	...	...	Ran but 12 miles. Examined 2 hours after finish
Z......	"	......	.....	....	....	....	...	...	...	......	27,700	.....	....	....	...	...	...	Sixteen years old.

* Preliminary red counts made two days before the race.

that the increase of leucocytes in the capillary blood after short cold baths was not maintained in the venous blood. There the leucocytes were normal.

Terminal Leucocytosis.

The leucocytosis of the moribund state, though by no means invariable, occurs in many cases, whether from the influence of a terminal infection or from stasis. When death is sudden or rapid, it does not occur. It seems to be analogous to the terminal rise of temperature seen at the close of many chronic non-febrile affections. The longer the patient is moribund the higher the count reaches. In pernicious anæmia the increase may be so great as to simulate lymphatic leukæmia. Such a case occurred in the writer's own experience (see also pages 136-137). The patient had presented the signs and symptoms of pernicious anæmia.

Slides taken on the day of death showed a ratio of one white to fifteen red cells, the small lymphocytes greatly predominating, but the autopsy revealed simply the lesions of pernicious anæmia. The differential count of 1,000 leucocytes on the day of death showed: Lymphocytes, 91.7 per cent; polymorphonuclear cells, 7.7 per cent; eosinophiles, 0.5 per cent. Four megaloblasts were seen while counting these. The total leucocyte count was about 60,000.

In ordinary cases the differential count shows an increase in the polymorphonuclear leucocytes. Thus in a case reported by Rieder, in which the leucocyte count rose during the last two days of life from 7,800 to 59,300, the polymorphonuclear cells constituted 87.5 per cent of the whole 59,300.

PATHOLOGICAL LEUCOCYTOSES.

For convenience' sake these may be divided as follows:

1. Post-hemorrhagic leucocytosis.
2. Inflammatory leucocytosis.
3. Toxic leucocytosis.
4. Leucocytosis in malignant disease.
5. Leucocytosis due to therapeutic and experimental influences.

1. Post-hemorrhagic Leucocytosis.

Within an hour after a large hemorrhage we find commonly a considerable increase (16,000-18,000). In hemorrhage from the stomach this disappears again, usually within a day or two, while in ordinary traumatic hemorrhage it persists longer. This last fact may perhaps be explained, as v. Limbeck suggests, by the local conditions in the wound rather than by the loss of blood in itself.

The polymorphonuclear leucocytes are usually increased relatively and absolutely as in other forms of pathological leucocytosis. Sometimes we have lymphocytosis (see page 118). The average of increase in the white cells is parallel in a general way to the anæmia produced in the individual, *i.e.*, it depends on his powers of recuperation rather than on the amount of blood lost. Its duration follows the same rule.[1]

2. *Inflammatory Leucocytosis.*

I use the term "inflammatory leucocytosis" rather than "leucocytosis of infectious diseases" because there is a considerable number of infectious diseases in which no leucocytosis occurs, while it accompanies almost all forms and cases of inflammation. Nevertheless I shall class under this heading some diseases in which inflammation plays but a very subordinate rôle.

I. Although *purulent and gangrenous* processes usually cause a higher count of white cells than *serous* processes, the amount of the exudation is not a measure of the amount of leucocytosis. It seems to depend rather on the resultant of two forces, viz., the severity of the infection and the resisting power of the individual. These factors may interact in various ways:

1. Infection mild: resistance good = small leucocytosis.
2. Infection less mild: resistance less good = moderate leucocytosis.
3. Infection severe: resistance good = very marked leucocytosis.
4. Infection severe: resistance poor = no leucocytosis.

This will be illustrated later under "Pneumonia" and under "Sepsis." Experiments on animals show that whereas moderate-sized doses of septic cultures, not sufficient to kill the animal, are followed by leucocytosis, larger doses, after which death follows speedily, do not raise the leucocyte count at all. Animals weakened by any cause show less leucocytosis to a moderate dose than strong animals.

If the individual reacts from the shock his leucocytes are increased again and rise above normal. If reaction fails, the leucocytes do not rise.

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[1] Further account of the blood after hemorrhage will be found on p. 126 *et seq.*

II. The course of the leucocytosis as regards both amount and duration shows, like the temperature chart, certain more or less characteristic differences in different cases.

III. In some diseases, *e.g.* in measles, in which the absolute number of leucocytes is not increased, we see a relative increase in the polymorphonuclear cells, pointing to the fact that influences are at work similar to those which produce an *absolute* increase.

IV. That the amount of exudation is not of itself a measure of the amount of leucocytosis is shown by the fact that erysipelas or scarlet fever may be accompanied by as high a count as the average count in pneumonia or empyema.

That purulent exudations usually have more effect on the white cells than do serous ones is due, I suppose, to the fact that a purulent inflammation usually means a severer infection.

V. No direct connection exists between leucocytosis and fever, many febrile affections running their course with a normal leucocyte count. When both leucocytosis and fever are due to the same causes they rise and fall together; but the correspondence is rarely accurate, and marked leucocytosis may exist without fever.

VI. Acute, rapidly spreading inflammations seem to produce a greater leucocytosis (other things being equal) than those in which the process is relatively chronic and stationary. For instance, an appendicitis, when well walled off and stationary, shows less increase in white blood cells than while its lesions are progressing. But peracute, overwhelming general sepsis may have no effect on the leucocytes, the reactive power of the organism being crushed.

VII. Most inflammatory leucocytoses are preceded by a temporary diminution in the number of leucocytes. This occurs in animals from *shock* of any kind (blows on the head, tying to the etherizing board), and it seems not unlikely that the cause is the same in all cases.

The following is a list of the more important inflammatory or infectious conditions in which leucocytosis appears:

1. *Infectious diseases with comparatively slight local inflammatory processes:*

(*a*) Asiatic cholera.

(*b*) Relapsing fever.

(*c*) Typhus fever (according to the majority of observers).

(*d*) Scarlet fever.
(*e*) Diphtheria and follicular tonsillitis.
(*f*) Syphilis (secondary stage).
(*g*) Erysipelas.
(*h*) The bubonic plague.
(*i*) Yellow fever (some cases).

2. *Infectious diseases with more extensive local lesions:*

(*a*) Pneumonia.
(*b*) Smallpox (suppurative stage)
(*c*) Malignant endocarditis, puerperal septicæmia, and all pyæmic and septicæmic conditions.
(*d*) Actinomycosis.
(*e*) Trichinosis.
(*f*) Glanders.
(*g*) Acute multiple neuritis (febrile stages).
(*h*) Acute articular rheumatism.
(*i*) Septic meningitis and cerebro-spinal meningitis.
(*j*) Cholangitis, cholecystitis, and empyema of the gall bladder.
(*k*) Acute pancreatitis.
(*l*) Endometritis, cystitis (some acute cases).
(*m*) Gonorrhœa.

3. *Local inflammatory processes:*

(*a*) *Abscesses* of all kinds and situations, such as:
Felon.
Carbuncle, furunculosis
Tonsillar and retropharyngeal abscess.
Appendicitis, phlebitis (some cases).
Pyonephrosis, perinephritic abscess, and pyelonephritis.
Osteomyelitis, empyema.
Psoas and hip abscess when not simply tuberculous.
Abscess of lung, liver, spleen, ovary, prostate.
Salpingitis and pelvic peritonitis, epididymitis.

(*b*) *Inflammations of the serous membranes*, including:
Pericarditis, peritonitis, arthritis (serous or purulent, non-tuberculous), conjunctivitis.

(*c*) *Gangrenous inflammations*, as of the
Appendix, lung, bowel, mouth (noma).

(*d*) Many inflammatory skin diseases, such as dermatitis, pemphigus, pellagra, herpes zoster, prurigo, some cases of universal eczema, etc.

3. *Toxic Leucocytosis.*

Under this heading I have grouped most of the conditions not obviously to be explained as infectious or inflammatory (though some may turn out to be such) and not due to malignant disease or therapeutic agencies. This classification is chiefly for convenience' sake and represents only a guess at the real explanation of the leucocytosis:

(*a*) Leucocytosis of illuminating-gas poisoning.
(*b*) " " quinine poisoning.
(*c*) " " rickets (many cases).
(*d*) " " the uric-acid diathesis, gout.
(*e*) " " acute yellow atrophy of the liver.
(*f*) " " advanced cirrhosis of the liver (some cases), especially with jaundice.
(*g*) " " acute gastro-intestinal disorders (ptomaïns?).
(*h*) " " chronic nephritis, usually in uræmic cases.
(*i*) Leucocytosis after injections of tuberculin and thyroid extract.
(*j*) " after injection of normal salt solution (intravenous).
(*k*) " after ingestion of salicylates, potassium chlorate, or phenacetin.
(*l*) " during and after prolonged chloroform narcosis (on the effects of narcosis upon the blood see page 253).

Possibly the leucocytosis of *acute delirium* and some cases of *acute mania* belong also in this group.

4. *Leucocytosis of Malignant Disease.*

Very likely this belongs more properly under one or another of the classes just mentioned Some observers think that it occurs only from the inflammation excited in the periphery of some malignant tumors; others that it is due to absorption of morbid products from the tumor itself; others again that it is to be accounted for by the cachectic state associated with the growth of the tumors. The details and conditions of its occurrence will be discussed later (page 428).

5. Leucocytosis Due to Therapeutic and Experimental Influences.

Pohl[1] found that most of the so-called tonics and stomachics produce a slight increase in the white cells in animals, particularly the vegetable tonics like tincture of gentian and oil of anise seed, while bismuth, bicarbonate of soda, and iron had no such effect. Quinine, caffeine, and ethyl alcohol gave likewise negative results. Von Limbeck found leucocytosis in men after oil of peppermint and oil of anise seed.

Binz[2] got the same results with camphor. In all these experiments the substances were given by the mouth.

Using subcutaneous or intravenous injections, Löwit experimented on animals with hemialbumose, peptone, pepsin, nucleinic acid, nuclein, extract of blood-leech, pyocyanin, tuberculin, curare, uric acid, urate of sodium, and urea. All but the last of these produce temporary decrease followed by increase of leucocytes.

Goldschneider and Jacob[3] used extracts of various organs. Extract of spleen, marrow, and thymus produced leucocytosis preceded, as in Löwit's experiments, by a brief diminution in the number of leucocytes, while extract of pancreas, thyroid, kidney, and liver had no effect.

Winternitz[4] injected a large variety of substances subcutaneously and found that the degree of leucocytosis was parallel to the degree of local reaction excited.

For example, neutral salts and weak acids or alkalies produced slight local inflammation and a leucocytosis of from forty to seventy-five per cent of the origial count. But irritants like turpentine, croton oil, nitrate of silver, sulphate of copper, mercury, antimony, digitoxin, etc., produced local suppuration (aseptic) and much greater leucocytosis (two hundred to three hundred per cent).

Pilocarpine and antipyrin have been found by von Jaksch and others to produce marked increase in the number of leucocytes when given subcutaneously. During the use of thyroid extract Richter (*Centralblatt f. inn. Med.*, 1896, p. 3) noted leucocytosis. Renzi and Boeri report leucocytosis (slight) after purgatives such as castor oil, podophyllin, and scammony. Schreiber (*Deut. Arch.*

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[1] Arch. f. exp. Path. u. Pharm., vol. xv., 1899.

[2] Arch. f. exp. Path. u. Pharm., vol. v., p. 122.

[3] Arch. f. Anat. u. Physiol., 1893, p. 567.

[4] Arch. f. exp. Path. u. Pharm., vol. xxxv., p. 77.

f. klin. Med., 1899, vol. lxii., p. 242) found that salicylic acid produced leucocytosis for the first few days of its administration.

Other drugs which have been reported to produce leucocytosis are potassium iodide, spermine, morphine, sodium salicylate, and phenacetin.

The transfusion of blood of normal salt solution has a like effect (see Bibliography in Da Costa).

A large number of observations on the effects of injections of bacteria or their toxins agree in the following results:

1. When the dose is very large the leucocytes are reduced, and the animal dies.
2. When the dose is not sufficient to kill the animal then temporary diminution in the leucocytes is soon followed by leucocytosis.
3. When the dose is slowly fatal the count of leucocytes oscillates up and down within wide limits.
4. Animals previously rendered immune to the poison injected show little or no leucocytosis.
5. Leucocytosis is more easily called forth and of greater extent in young animals.
6. Most pathogenic organisms act similarly, but bacilli and toxins of tuberculosis as a rule cause no leucocytosis.
7. There is no evidence that any one variety of leucocyte is attracted by any particular bacillus or toxin.

In the above sketch of therapeutic and experimental forms of leucocytosis no attempt has been made to give anything but the more interesting and important outlines of the immense amount of work done.

Cell Structure of the Leucocytes in Leucocytosis.

Hitherto we have spoken as if leucocytosis meant only an increased *number* of the normal cells, but one cannot study the cell forms in extensive pathological leucocytosis without noting in many cases *qualitative* changes in the individual cells. These are chiefly:

1. A greater or less approximation of the nuclei of polymorphonuclear neutrophiles to the appearances of the myelocyte nucleus. As will be mentioned later under leukæmia, we find in every blood containing many myelocytes numerous cells whose nucleus is on the border line between the myelocyte and the polymorphonuclear stage, so far as appearances go. Now in leucocytosis we find the same "border-line" cells in smaller numbers, the *likeness* to the

myelocyte sometimes passing into *identity* in one to three per cent of the cells.

2. Türck's "Reizungsformen" or "stimulation cells" in which the protoplasm of the cell (which is in other respects like a large lymphocyte) shows a greater or less approximation to the appearance of myelocyte protoplasm, *i.e.*, a diffuse violet or purple color exactly as in the myelocyte but *non-granular.* Engel makes a separate variety of this cell, giving it the useless name of "mononuclear cell." Weil calls it the "non-granular myelocyte." Türck considers its presence in the circulating blood to indicate a *stimulation* of the marrow by the toxins of disease, resulting in the passage of this—supposedly immature—cell into the blood.

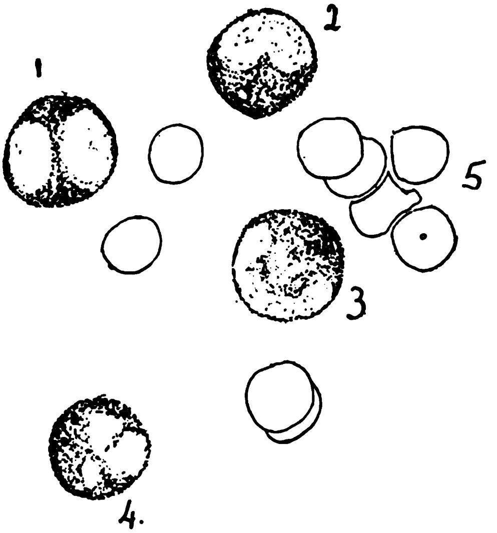

FIG. 26.—Atypical Leucocytes seen in Leucocytosis. 1, Leucocytes with polar arrangement of nuclei (mitosis ?); 2 and 3, leucocytes with nuclei resembling those of myelocytes; 4, leucocyte containing two kinds of granules.

3. Other finer changes, such as the number, size, and staining power of the neutrophilic granulations, polar position of the nuclei, etc. (see Fig. 26), require further study.

Changes like the above militate against the idea that leucocytosis is simply a matter of the distribution of fully formed leucocytes in the peripheral or internal vessels.

For an account of iodophilia or the iodine reaction in the polynuclear leucocytes during suppurations see page pages 42–43.

Absence of Leucocytosis.

It is of fully as great a practical assistance to us to know that in certain infective diseases leucocytosis is regularly absent as to know those conditions in which it is to be expected. Among the most important diseases in which leucocytosis is conspicuously absent are:

(*a*) Typhoid fever and "paratyphoid" infections.
(*b*) Malaria.
(*c*) Grippe (most cases).
(*d*) Measles.
(*e*) Rötheln and mumps.
(*f*) Malta fever.
(*g*) Cystitis.
(*h*) Tuberculosis, including—
    Incipient phthisis.
    Miliary tuberculosis.
    Tuberculous peritonitis.
    " ostitis and periostitis.
    " pleurisy.
    " pericarditis.[1]

In some of these affections, notably in miliary tubercle and the later weeks of typhoid, the leucocytes are diminished. Further details will be given under the special diseases.

LEUCOPENIA.

Definition.—A diminution in the number of white cells in the peripheral circulation as compared with the number normal for the given individual.

1. The effects of starvation and malnutrition in producing leucopenia have already been described. Such leucopenia is usually associated with lymphocytosis (see below). Cancer of the gullet is an example of this class.

2. Short hot baths or prolonged cold baths produce temporarily the same result (Winternitz, *loc. cit.*).

3. Most of the infective diseases in which there is no leucocytosis are sometimes characterized by leucopenia, *e.g.*, grippe, measles,

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[1] Tuberculous *meningitis* often does show leucocytosis (*vide infra*, p. 303).

miliary tuberculosis, and other forms of pure tuberculous infection, malaria, and especially typhoid, in the later weeks of which it is almost invariable, and is accompanied by lymphocytosis. In a case of glandular tuberculosis with bronchopneumonia Vaquez and Ribierre (Soc. Méd. d. Hôp., 1900, p. 914) report a great diminution both of red cells (to 1,000,000) and of leucocytes (to 2,300) the loss involving solely the polynuclears, which were reduced to 184 per cubic millimetre (eight per cent), while the lymphocytes remained nearly normal, 2,116 per cubic millimetre (ninety-two per cent).

P. K. Brown has recently reported a fatal case of infectious pharyngitis with intense and continued leucopenia. When a case of leukæmia is complicated by an infective disease (pneumonia, septicæmia) the number of leucocytes may fall below the normal. In a case recently occurring at the Massachusetts General Hospital in which a lymphatic leukæmia was terminated by septicæmia from glandular suppuration, the white cells fell gradually from 40,000 three weeks before death to 419 per cubic millimetre on the day of death.[1] The differential count was unchanged (lymphocytes = ninety-eight per cent).

4. In pernicious anæmia the count is usually very low and may fall below 1,000 cells per cubic millimetre Other severe types of anæmia (rachitic, syphilitic, post-hemorrhagic) may produce the same result.

5. Splenic anæmia or the splenic form of Hodgkin's disease is often associated with marked leucopenia.

6. Medicinal leucopenia—following the injection of ergot, tannic acid, sulphonal, atropine, agaracin, and some other drugs, has been described by Bohland (*Centralb. f. inn. Med.*, 1899, vol. xx., p. 361).

LYMPHOCYTOSIS.

Lymphocytosis is an absolute and relative increase in the circulating lymphocytes. The increase is relative to the number of lymphocytes normal for the individual. When lymphocytosis and an increase of the total leucocyte count are present we cannot distinguish the blood from that of lymphatic leukæmia, and the distinction must depend upon the course and symptoms of the case.

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[1] Koblank (Dissert., Berlin, 1898) could find but *one* leucocyte in twenty stained cover-glass preparations from the blood of a case of epilepsy. No count was made. In Brown's case (American Medicine, April 19th, 1902) the leucocytes sank to 260 per cubic millimetre before death.

1. Such a condition (relative to the adult) occurs *in healthy infants' blood* and in many diseases of infancy, the blood seeming to have a tendency to return to the infantile type. This is especially true of cholera infantum, rickets, and congenital syphilis. Anything that retards the infant's normal gain in weight or general development retards its blood development as well.

2. *Pertussis,* as Meunier has recently shown, is accompanied by a very marked lymphocytosis, the lymphocytes being quadrupled while the polynuclear cells are doubled. The increase is absolute as well as relative (see pages 107 and 220).

Variola also shows lymphocytosis according to Weil.

3. *Hereditary syphilis* is perhaps the best-known cause of relative lymphocytosis in children. *Scurvy* may produce the same result. Dividing the anæmias of children into two groups, those that do and those that do not produce leucocytosis, it appears that the great majority of those whose total leucocyte count is normal show a relative lymphocytosis. This is the case irrespective of whether there is enlargement of the spleen or not. Sometimes the smaller, sometimes the larger lymphocytes are in the majority. Often no division between the two kinds is possible.

4. In adults some forms of *debility* may be associated with an increased *percentage* of lymphocytes, due in fact to the *absolute diminution of the neutrophiles.* This should be distinguished from true lymphocytosis. The same false appearance of lymphocytosis may be seen in hæmophilia, goitre, cervical adenitis, and other conditions involving a diminution of the polynuclear neutrophiles, *in chlorosis, pernicious anæmia, Graves' disease* and the anæmia secondary to *syphilis,* in the later weeks of typhoid fever and in lactation.

5. After the administration of thyroid extract, tuberculin, pilocarpine, or quinine hydrochlorate subcutaneously.

6. The larger forms of lymphocytes are in increased in malaria, in some splenic tumors (chronic "ague cake"), and especially in the post-febrile stage of measles; also in many of the same diseases in which the small lymphocytes are increased.

7. The most marked absolute lymphocytoses known to me (excluding leukæmia) occurred in two cases of pertussis-pneumonia in infancy. One case occurred at the Massachusetts General Hospital in 1894—in a child of six, who passed through an attack of broncho-

pneumonia with uneventful recovery, the only peculiarity of the case being the marked increase of white cells running up to 94,600, *sixty-nine per cent of which were lymphocytes.* During convalescence the blood became normal and the child left the hospital entirely well. In 1900 we had a similar case in a baby of fifteen months, well until seized with paroxysms of coughing four days before entrance.[1] The spleen and glands were normal. There were no hemorrhages and no anæmia. The blood showed

	White cells.	Per cent polynuclear.	Per cent lymphocytes.	Per cent. eosinophiles.	Remarks.
First day .	103,000	35	64.5	0.5	Red cells normal. No nucleated forms.
Third day.	104,850				
Fifth day.	185,000!				
Sixth day.	Death. No autopsy.				

Since reading Meunier's account of the enormous lymphocytosis of *whooping-cough* I have believed these two cases to have been atypical whooping-cough. These cases will be referred to later in the account of the blood of pneumonia.

Diagnostic Value of Lymphocytosis.

1. I have already suggested that the degree of health in persons not organically diseased might perhaps prove to vary directly with the percentage of polymorphonuclear cells in the blood.

2. In children the same percentage is to a certain extent a measure of the child's degree of development—causes of leucocytosis being excluded, and the percentage normal for a child of the patient's age being taken as the standard.

3. Absolute lymphocytosis in the presence of glandular tumors is our mainstay in the diagnosis of lymphatic leukæmia, but whooping-cough must always be remembered as a source of error.

EOSINOPHILIA.

Definition.—An increase in the number of eosinophiles in the circulating blood.

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[1] A similar case has recently been reported by Steven (see page 221).

Physiological Eosinophilia.

There is no constant eosinophilia either in infancy or during menstruation, as the researches of Carstanjen have shown; but at these periods the number of eosinophiles is subject to remarkable oscillation, which no doubt has given rise to the impression that they are regularly increased.

Among the causes of *pathological eosinophilia* are:

1. *Bronchial Asthma and Fibrinous Bronchitis.*—During paroxysms the eosinophiles are plentiful in the sputum and in the mucous membrane of the upper air passages as well as in the blood. In the case quoted from Billings (see page 377) there were 53 per cent of eosinophiles in a leucocyte count of 8,300. Gabritschewsky reports 22.4 per cent in asthma.

2. *Acute and Chronic Skin Diseases.*—The most marked cases are those reported by Lazarus (60 per cent of eosinophiles in *urticaria* widely distributed), Zappert (33 per cent, or 4,800 eosinophiles per cubic millimetre in *pemphigus*), and by Canon (17 per cent in prurigo and psoriasis). In *dermatitis herpetiformis* high eosinophile counts are reported by Leredde and Perrin, by Brown, and by myself (see page 505).

3. *Helminthiasis.*—*Trichinosis* and *uncinariasis* are the members of this group which have been most thoroughly studied, and in both of them eosinophilia is marked and constant (see pages 490 and 497), but of late evidence is fast gathering to show that filariasis, Bilharzia disease, hydatid disease, and others, due to animal parasites, are likewise associated with eosinophilia.

Bücklers, working under Leichtenstern, has established the interesting fact that "*all* varieties of helminthides, from the harmless oxyurides to the pernicious ankylostoma, may bring about an increase of eosinophiles in the blood, often to an enormous extent." Bücklers reports 16 per cent of eosinophiles in oxyurides, and 19 per cent in ascarides, and Leichtenstern has quite recently found 72 per cent of eosinophiles in ankylostomiasis, and 34 per cent in a case of tænia mediocanellata (Ehrlich and Lazarus, page 103).

4. *Post-Febrile.*—At the height of most acute infectious fevers (except scarlet fever and sometimes rheumatic fever) the eosinophiles are greatly diminished or absent. In the post-febrile period, however, abnormally high percentages of eosinophiles are often found.

Türck found 5.67 per cent (430 absolute) after pneumonia; 13.8 and 9.37 per cent (970 absolute) after rheumatism. Zappert found 20.34 (1,486 absolute) after malaria; 26.9 per cent (3,220 absolute) after tuberculin reaction fever. Grawitz found 90 per cent (!) (41,000 absolute) after tuberculin reaction fever (see page 292).

5. *Malignant Tumors.*—Various authors (Weiss, Palma, Rieder) have observed a slight eosinophilia in connection with the cachexia of malignant disease. It is, however, of moderate degree and seldom exceeds seven to ten per cent.

In Reinbach's study of 40 cases there were 4 with eosinophilia as follows: Sarcoma of the forearm, eosinophiles 7.8 per cent; sarcoma of the femur, eosinophiles 8.4 per cent; malignant tumor of the abdomen, eosinophiles 11.6 per cent; lymphosarcoma of neck with ulcerative endocarditis and metastases in the bone marrow, eosinophiles 48 per cent (60,000 absolute) (see pp. 457–458).

Among my cases there is one of generalized sarcoma with eosinophiles 12.4 per cent (2,108 absolute). Zappert quotes a case of lymphosarcoma with 17.7 per cent (2,077 absolute) and 2 cases of cancer (uterus and stomach) with 11 per cent (860 absolute) and 8.5 per cent (535 absolute).

6. *Compensatory Eosinophilia.*—Ehrlich's researches appear to show that when the function of the spleen is abolished, either by splenectomy or by disease, a late compensatory eosinophilia occurs.

7. *Medicinal Eosinophilia.*—After the administration of camphor, v. Noorden observed an eosinophilia of 9 per cent in 2 chlorotic girls. Phosphorus poisoning is also said to cause eosinophilia, and Taylor refers to nuclein and pilocarpine as possessed of similar properties.

8. *Myelogenous Leukæmia* (see page 164).

9. *Eosinophilia in Hæmatoma, Hemorrhagic Exudations, and Purpura.*—Klein (*Centralbl. f. inn. Med.*, January 28th, 1899)

Case.	Date.	Red cells.	White cells.	Per cent hæmoglobin.	Per cent polynuclears.	Per cent eosinophiles.	Per cent lymphocytes.
1........	March 29	3,800,000	11,800	45	71.7	12.5	15.8
	April 4	....	6,200	....	56.5	37.5	6.
	April 11 (1893)	....	8,150	....	44.	40.	16.
2........	April 9	....	....	....	69.1	6.5	24.3
	April 21 (1894)	....	9,189	....	65.1	16.1	18.7

reports two cases of hemorrhagic pleural exudation with a very large number of eosinophiles (74 to 76 per cent) in the exudate and a marked increase of circulating eosinophiles:

Perhaps of a similar type is the eosinophilia exemplified in the following report from a case of simple purpura in a girl of eight: White cells, 18,000; eosinophiles, 17.5 per cent; polynuclears, 44 per cent; lymphocytes, 39 per cent.

10. *Eosinophilia in Benign Ovarian Disease.*

Neusser, in 1892, stated the eosinophiles are increased in diseases of the female genitals. Kopp (Dissert., Würzburg, 1894) could find but five out of sixteen cases of ovarian tumors showing eosinophilia, but Voswinkel (*Monatschr. f. Gebürtsh. u. Gynäkol.*, 1898, p. 413) has carefully studied 126 cases of pelvic disease with the following results:

I. Diseases of the Fallopian tubes, endometritis, and myoma uteri (31 cases) show a normal percentage of eosinophiles and no myelocytes.

II. *All severe ovarian diseases* (excepting in febrile stages and excepting also cancer of the ovary) *are associated with eosinophilia* and an increased percentage of polynuclear cells (40 cases). Even if the ovary is mostly destroyed eosinophilia is usually present (10 out of 18 cases).

III. In cancer of the uterus the eosinophiles may be normal, increased, or diminished (19 cases).

Diminution in Eosinophiles.

1. During severe muscular exertion.
2. After castration (Neusser).
3. In febrile stages of pneumonia, grippe, typhoid, diphtheria, sepsis, and most infectious diseases accompanied by leucocytosis. That this is not due simply to the presence of fever is shown by the fact that in malaria and scarlet fever, despite high fever, eosinophiles may be increased.
4. In the moribund state eosinophiles are diminished or absent.
5. Malignant disease, hemorrhage, and most of the other causes of leucocytosis also diminish the eosinophiles.

Diagnostic and Prognostic Value of Eosinophilia.

In trichiniasis eosinophilia is of great diagnostic value.

Neusser has suggested the following points:[1]

1. In the diagnosis between puerperal mania and puerperal sepsis, eosinophilia points to the former.
2. Between a tumor connected with the genital system and one not so connected, eosinophilia points to the former.
3. In determining whether a given case of hysteria, neurosis, or psychosis is likely to be benefited by castration, the presence of eosinophilia favors the operation.
4. In malignant disease an eosinophilia points to a metastasis in the osseous system (tumors of the spleen are not included in this rule).
5. In cases of doubtful syphilis eosinophilia combined with lymphocytosis (see above) speaks in favor of syphilis.
6. The diagnosis of any obscure form of "uric-acid diathesis" is helped by finding an increase of eosinophiles.
7. In distinguishing malignant liver disease from other liver disease eosinophilia points to the latter.
8. In the *prognosis* of chlorosis, eosinophilia is favorable.
9. In the prognosis of scarlet fever and scarlatinal nephritis the greater the eosinophilia the better the prognosis.
10. After hemorrhage increased eosinophiles show active regeneration of blood and good prognosis.
11. In pernicious anæmia eosinophilia is favorable for the same reason.

MYELOCYTES.

The occurrence of the myelocyte of Ehrlich in the circulating blood is almost always to be looked upon as pathological, that is, as the intrusion of a variety of leucocyte naturally a stranger to the circulating blood and a permanent inhabitant of the marrow. Among hundreds of specimens from healthy persons I have seen but one typical myelocyte.

1. The largest number of circulating myelocytes occurs in myelogenous leukæmia (see page 161).
2. In all conditions associated with stimulation of the bone marrow—that is, in all diseases accompanied by well-marked leu-

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[1] For none of which I can vouch.

cocytosis or by severe anæmia of any type—myelocytes in small numbers may frequently be found. Thus I have found them in most cases of pernicious anæmia and of malignant disease with leucocytosis. Türck finds them in most acute infections, even in typhoid with subnormal leucocyte count. Engel has noted their frequent presence in diphtheria, while Neusser[1] has noted them in various toxic conditions such as puerperal mania, osteomalacia, uræmia, carbonic-acid poisoning, Basedow's disease, diabetic coma. Others have recorded their occurrence in rickets, syphilis, phthisis, general paralysis, etc.

The common elements in these various diseases are anæmia and leucocytosis. In fact, I do not know of any of the very numerous diseases and conditions associated with leucocytosis in which myelocytes have not been found. Accordingly it seems to me reasonable to class them as signifying a marrow stimulation, and as much akin to Türck's "stimulation forms" (see page 103).

As a rule I think the presence of myelocytes indicates an acceleration of those marrow functions by which granular leucocytes are furnished to the blood. Such an acceleration may be supposed to take place in leucocytosis, leukæmia, and severe anæmia, which are the chief conditions in which myelocytes appear in the blood.

MAST CELLS.

1. Many of the same causes which increase eosinophiles (*e.g.*, animal parasites, skin diseases) also increase the mast cells slightly.
2. A. E. Taylor (Contrib. of Pepper Labor., Phil., 1900, p. 148) has noted an increase in one case of carcinoma, one of gonorrhœa, one of mycosis fungoides, and two of septic bone disease.
3. The most constant and extensive increase of mast cells is found in myelogenous or mixed-cell leukæmia.
4. Osler records five to six per cent in a case of "splenic anæmia." In one of my cases they numbered four per cent (632 per cubic millimetre).
5. Zollikoffer (Dissert., Berne, 1899) has noted increase of mast cells in hysteria, in sciatica, and in articular rheumatism without fever. No counts are given.
6. Bigart (*La Sem. Méd.*, December 31st, 1902) reports 20.6 per cent of mast cells in a case of Hanot's cirrhosis.

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[1] Cited in Klein: Volkmann's "Samml. klin. Vorträge," December, 1893.

CHAPTER IX.

GENERAL PATHOLOGY OF THE BLOOD AS REGARDS HÆMOGLOBIN, FIBRIN, LIPÆMIA, MELANÆMIA, AND HEMORRHAGE.

HÆMOGLOBIN.

As stated above, the hæmoglobin may increase and diminish in lines parallel to those of the red cells. In that case we suppose the amount of hæmoglobin per corpuscle to be normal and the *color index* or *valeur globulaire* is said to = 1. When the hæmoglobin is diminished more than the count of corpuscles, we may say that the color index is less than 1. For example, if a man has 5,000,000 red cells per cubic millimetre and only 50 per cent of hæmoglobin, we estimate the color index by simply reducing the count of cells to a stated percentage (5,000,000 cells = 100 per cent of cells) and dividing this percentage into the hæmoglobin percentage—*i.e.*, $\frac{50}{100} = 0.5$ = the color index. Therefore 4,000,000 red cells (= 80 per cent) with 60 per cent of hæmoglobin give a color index of $\frac{60}{80} =$ 0.075.

The color index rarely goes above 1, except in pernicious anæmia (see below). Here it may be as high as 1.7. As a rule, when the red cells are above the normal, the hæmoglobin rises equally, sometimes it lags behind a little, but rarely if ever does it rise higher than the cells.

In most anæmias, as has been pointed out, the hæmoglobin suffers markedly before any considerable loss of red cells takes place. In other words, the corpuscles seem to get thin before they die, and except in malaria, hemorrhage, and a few other cases they are not destroyed while in the full vigor of health.[1]

The loss of hæmoglobin is loss of albumin, the chief constituent of the cells, and hence is usually loss of weight.

In general the changes in the hæmoglobin are best studied in connection with changes in the count of red cells, and so far as they have not already been mentioned will come in under the various special diseases.

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[1] This is of course not literal. There is no reason to suppose that good-sized corpuscles get smaller. It is more likely that a smaller generation is sent out by the blood-making organs.

FIBRIN.

The fibrin network to be seen in normal blood during coagulation (see page 52) is increased in a considerable number of conditions. Hayem has studied these minutely, and described several varieties of arrangement of fibrin fibres as characteristic of special diseases, that is, studied fibrin qualitatively as well as quantitatively, and also as regards the rapidity of its formation.

The rate of fibrin formation is often not the same as the rate of coagulation. It is not parallel to the number of leucocytes or blood plates, at least not in all cases (malignant diseases, scurvy).

In a general way we expect increased fibrin in infectious and inflammatory diseases, but there are notable exceptions to this. The greater the exudation and the freer it is (in a cavity or on the surface) the thicker the fibrin network, while so-called interstitial inflammations or such conditions as parenchymatous nephritis show little increase in fibrin. The seat of the lesions has no considerable influence, except as it modifies the nature of the lesion. An abscess in one place has the same effect as an abscess elsewhere, provided it is equally free or equally confined, and of the same contents.

Tuberculosis does not increase fibrin if uncomplicated. Leucocytosis and fibrin behave alike in many respects, especially in relation to the vigor of resistance which the individual opposes to a given infection. When the individual is so weakened that he does not react well against the infection, the leucocytes and fibrin are but slightly increased, whereas in a vigorous individual the same infection would have markedly increased both fibrin and leucocytes. But neoplasms raise the count of leucocytes without changing the amount of fibrin.

In a general way fibrin increases and decreases as fever does, but often persists after fever is gone.

The most marked fibrin networks are seen in pneumonia, acute articular rheumatism, suppurative diseases, and in scurvy. In erysipelas it follows the leucocytes (increased in severe, not in mild cases). In the early days of grippe it is increased.

The fever of hysteria or chlorosis shows no increase of fibrin, and post-hemorrhagic anæmia with or without fever shows none.

Fibrin is diminished in pernicious anæmia, not increased in leukæmia, typhoid, malaria, malignant disease, non-suppurative diseases of liver, nephritis (except interstitial nephritis, in which it may be increased), heart disease, purpura, hæmoglobinuria (sometimes decreased).

The most valuable point about the fibrin appears to be the absence of any increase in malignant disease whereby a diagnosis between the affection and a suppuration may be helped. Otherwise the information given by it is chiefly confirmatory of impressions given by other features in blood examination.

LIPÆMIA.

The blood invariably contains small quantities of fat, especially during digestion (v. Jaksch[1]).

In the blood of persons suffering from a variety of diseases such as phthisis, diabetes mellitus, obesity, alcoholism, nephritis, and in some dyspnœic conditions, suppressed menses, pregnancy, icterus, typhus, malaria, mental disease, diseases of the heart and pancreas, as well as in health, fat is occasionally to be seen in considerable quantities. Grawitz[2] finds that if the blood is collected in a fine capillary tube, and this is kept in a horizontal position for some time, fat rises to the surface like cream, and can be seen with an oil-immersion lens in the form of fine drops. Gumprecht[3] demonstrated it with osmic acid, which stains the fat drops black, and proved them to be fat by dissolving them in ether, xylol, etc.

Lipæmia has no special significance so far as is known, and is not characteristic of the diseases above mentioned. Its cause is unknown.

[In almost any preparation of the fresh blood fat drops are to be seen unless the patient's skin is washed with alcohol before puncturing. Even with these precautions a few drops may often be seen in healthy people's blood.]

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[1] "Klin. Diagnostik," p. 75 (English translation).

[2] *Loc. cit.*, p. 160.

[3] Deut. med. Woch., 1894, No. 39.

MELANÆMIA.

In malaria the occurrence of a black pigment in the leucocytes which have taken plasmodia into themselves is generally to be seen during and shortly after a paroxysm. Pigment free in the blood is to be seen only at the moment of segmentation among the new generation of parasites. The same condition has been observed in relapsing fever and in persons suffering from melanotic malignant tumors, the pigment being always in the white corpuscles. Presumably it must at some time be free in the plasma, but it is rarely if ever seen outside the cells.

In Addison's disease Tschirkoff[1] observed pigment in the leucocytes.

HEMORRHAGE.

Women can stand a greater hemorrhage than men. Children, on the other hand, succumb to comparatively slight hemorrhages (*cf.* Blood in Infancy, page 510). Individual differences make a great difference in the ability to survive hemorrhage, and no exact amount of blood can be stated as the maximum that any one can lose and yet survive.

Changes in the Blood Resulting from Hemorrhage.

The red cells and hæmoglobin of course suffer proportionately at first; later the hæmoglobin in the newly formed cells is always deficient (see below).

The striking point in the blood after hemorrhage is the evidence it gives us that even before the hemorrhage has ceased the other tissues begin to contribute fluid to make up the *volume* upon which life depends. The serum is markedly diluted by this fluid, but still serves to give the heart something to contract on and so prevents blood pressure from falling as fast as it otherwise would do. Were it not for such contributions from neighboring tissues the organism could sustain but slight hemorrhage without succumbing at once. We have then after hemorrhage a diluted or hydræmic blood, even though we do not assist the efforts of nature by contributing fluid by intravenous or rectal injection. Dock[2] reports a case due to epistaxis in which the count fell to 357,600 per cubic millimetre The counts in this case were as follows:

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[1] Zeit. f. klin. Med., vol. xix., 1891.

[2] Dock: Trans. of Association of American Phys., 1899, p. 180.

Date.	Red cells.	White cells.	Hæmoglobin.	Polynuclears.	Small lymphocytes.	Large lymphocytes.	Polynuclear eosinophiles.	Mononuclear eosinophiles.	Myelocytes.	Erythroblasts per cu. mm.	Remarks.
Jan. 12.....	1,120,000	13,300	25%	67.3	6.2	21.4	2.6	0.3	0.3	2,605	
" 16.....	....	30,500	....	69.0	2.1	14.1	2.5	..	..	6,900	
" 19.....	....	......	....	60.1	2.7	27.2	3.3	..	3.0	....	48 megaloblasts out of 500 erythroblasts.
" 20.....	357,600	49,600	20%	....	....	....	....	..	..	22,000	
" 26.....	820,000	48,000									
" 22.....	....	......	....	54.0	6.9	25.7	2.3	.3			
" 25.....	760,000	35,000	....	57.2	7.9	23.5	1.8	.4	9.2	14,000	
" 27.....	Death										

All the cover-glass films showed a few red cells in mitosis. There is here an absolute increase of *all* varieties of leucocytes, with a high color index and enormous numbers of nucleated red cells.

Coagulation increases in rapidity the more blood is lost, so that after severe hemorrhage it takes place almost instantly. This is probably due to the great increase in the blood plates which most observers have noted after hemorrhage.

BLOOD REGENERATION.

The regeneration of the blood after hemorrhage may be taken as typical of the same process in anæmia from other causes.

The length of time needed for full restoration to normal depends not merely on the (*a*) *amount* of blood lost, but also on the (*b*) age and nutrition of the patient as well as upon (*c*) the methods of *treatment* carried out and the existence of (*d*) other disease (typhoid, malignant disease, phthisis, etc.).

Allowing for these other conditions we may say that, other things being favorable, the loss of:

I. Less than 1 per cent of the blood mass is made up in 2 to 5 days.
II. From 1 to 3 " " " " " " 5 " 14 "
III. " 3 " 4 " " " " " " 14 " 30 "

The last amount means a very severe hemorrhage. Few surgical operations involve the loss of over three per cent, and after such accordingly we expect the blood to be normal again in two weeks, provided the individual is otherwise sound (see Malignant Disease, page 425). Grawitz records a gain of 2,000,000 red cells in two weeks after a gastric hemorrhage (ulcer).

Young, well-nourished persons are of course quicker in making up losses than the old and weak.

Blood Condition During Regeneration.

1. *Red Cells.*—(A) As previously mentioned, the hæmoglobin becomes relatively low as soon as the regenerative process is well established, and as recovery progresses the red cells are almost always normal in numbers for some time before the stature, weight, and color of the individual cells is what it should be. A color index of 0.50–0.60 is not unusual—in short, what some call a "chlorotic" condition of the blood.

(B) Qualitative changes are those already described on page 78, namely: (*a*) Deformation in size and shape with an average diminution in size; (*b*) polychromatophilic cells; and (*c*) nucleated corpuscles. These latter are almost exclusively of the normoblast type, but an occasional megaloblast has been observed.

Blood Crisis.—Von Noorden was the first to notice that in some cases nucleated corpuscles are to be found in the circulation in great numbers for a few hours only, the blood examination both before and after showing few or none at all. The name of "blood crisis" has been given to these sudden outpourings of nucleated red cells; they are to be observed during recovery from various forms of anæmia.

2. *White Cells.*—Immediately after a loss of blood we can usually find a decided *leucocytosis* despite the dilution of the blood (see above, Post-hemorrhagic Leucocytosis).

This leucocytosis may not differ from those occurring from other causes. The percentage of polymorphonuclear cells is usually increased, and the eosinophiles often disappear or, as in Dock's case, just referred to, all varieties of leucocytes may be increased, or, again, as pointed out by Stengel, we may have a lymphocytosis after hemorrhage, either from the start or following a polynuclear leucocytosis. In his case the percentages were: Polynuclears, 43.5; lymphocytes, 43.5; transitionals, 10; eosinophiles, 2.8. A case of anæmia from bleeding piles, in which the red cells were 2,723,000 and the hæmoglobin 35 per cent, showed in a total leucocyte count of 4,200, 69 per cent of small lymphocytes and only 28 per cent of polymorphonuclear cells. Leucocytosis, if present, is rarely very high, seldom reaching over 30,000. It is not invariably present, or, if present, sometimes is of very short duration. Thus in a patient whose red cells were reduced to 3,200,000 by a profuse uterine hemorrhage the white cells counted next day were only 8,000; while in the next bed of the hospital was a woman crushed in a railroad accident whose red cells were 1,280,000, and the white cells 28,000, the usual state of things.

The leucocytes may be increased even by a *cerebral hemorrhage* which is not large enough considerably to affect the red cells in most cases. Obviously some other influence is at work in these cases (see page 385).

The effect of transfusion (intravenous saline solution) is apparently at first to increase the leucocytosis.

D——, a patient with traumatic rupture of the urethra, had had severe hemorrhage for forty-eight hours before it was checked at 1 P.M., November 1st, 1895. At 4 P.M., his pulse being 165, the count showed red cells, 3,304,000; white cells, 10,400. He was at once given a pint of sterilized normal salt solution by intravenous injection under the strictest asepsis. Ten minutes after the transfusion the leucocytes numbered 32,400. One hour later they were 24,700, and the red cells 3,632,000. Four hours later, leucocytes, 31,900; red cells, 3,046,000. The later counts were as follows:

		Red Cells.	White Cells.
November	2d: good pulse	3,608,000	34,600
"	2d (5 P.M.): good pulse	2,944,000	30,200
"	3d (4 P.M.): good pulse	2,928,000	15,800
"	13th	3,360,000	16,600

A good recovery was made.

CHRONIC HEMORRHAGE.

Piles, uterine disease, hæmophilia, purpura, and other causes may produce a long-standing drain on the blood.

Some patients apparently can lose a little blood almost daily for years without acquiring any severe anæmia, and if the individual is otherwise sound and does not suffer from an underlying disease like phthisis, cancer, or nephritis, he can probably go on for a long time without showing any bad effects from the repeated small hemorrhages. *How* much he can stand we have no way of judging, for we cannot measure the amount of blood lost. When, however, such small repeated losses *do* produce an anæmia, regeneration is apt to be much slower than after a single large hemorrhage. The longer the drain has been going on the poorer the chance for recovery, and the slower the latter will be if it does take place.

Gain in body weight does not always mean gain in corpuscle substance as well (see Malignant Disease, page 425).

BOOK II.

SPECIAL PATHOLOGY OF THE BLOOD.

PART I.

CHAPTER I.

THE PRIMARY ANÆMIAS.

I. THE BLOOD IN PERNICIOUS ANÆMIA.

1. *Volume and Oxygen Capacity.*—J. Lorrain Smith, studying the blood of seven cases by the carbonic-oxide method, concludes that "absolute loss of oxygen capacity (= hæmoglobin), which in chlorosis practically does not occur, is here of primary importance. Whereas, in chlorosis, the oxygen capacity is 95 per cent of the normal, here it averages 48 per cent, and in one case was but 28 per cent."

The volume of blood is sometimes markedly increased, sometimes normal, sometimes diminished. Patients with a large volume of blood seem to feel worse than those with normal volume, even when the hæmoglobin percentage and count of corpuscles are approximately the same. In the remissions of the disease the volume may be rapidly reduced. So, for example, 4,305 c.c. with 1,100,000 red cells per cubic millimetre and later (in remission) 2,775 c.c. with 3,104,000 red cells per cubic millimetre.

2. *Gross Appearances.*

(*a*) The drop as it emerges from the puncture is often excessively pale and watery, but not more so than may occasionally be seen in secondary anæmia or chlorosis. Sometimes it is not nearly so pale as in other cases with equally low counts, a fact which may be due to the increased color index sometimes present (see below).

In several early cases I have seen the blood as red as normal.

Another appearance, which I have frequently observed in this and other anæmias, is an uneven, streaked color in the drop, as if the cells were unequally divided in the plasma.

(*b*) As striking as the color of the drop is its great fluidity; the rapidity with which it slips off the ear or finger often makes it difficult to suck it up in time. It is usually very slow in coagulating. When drawn the blood does not separate into serum and clot, even after the lapse of seventy-two hours (Lenoble).

(*c*) The fresh specimen in most cases shows no rouleaux formation, and a marked diminution in blood plates and fibrin. Hayem says: "This double lesion, rarity of blood plates and loss of retractility on the part of the clot, is, according to my latest observations (1900), the *most* characteristic sign of this form of primary anæmia." I have no experience on this point.

There are usually great variations in the size and shape of the corpuscles with a tendency to an oval shape and an increase in the average diameter. Not infrequently the deformed corpuscle shows active pseudo-amœboid motions of its projecting points or of the cell as a whole. The great lack both of red and white cells is noticeable even in the fresh specimen.

Red Cells and Hæmoglobin.

(*a*) Quantitative changes (see Table I.). The average count of red cells in the one hundred and ten cases of my table is about 1,200,000, which may be taken as the average count in patients seen at the stage of the disease at which they feel sick enough to seek medical advice.[1] We very rarely get an opportunity to examine the blood in the early stages of the disease, so that we have to judge of them chiefly from the evidence given during the remission so commonly observed. In the relapse following such a remission the blood count may fall from 5,000,000 to 1,000,000 in a period of from six weeks to six months. In the later stages of the disease 500,000 red cells per cubic millimetre is not rare, and if the diminution has been gradual, the patient may be up and about and able to do light work with a count no greater than this. I watched such a case in the wards of Dr. F. C. Shattuck at the Massachusetts General Hospital in 1892, in which for several weeks the blood count remained at or near 500,000, yet the patient was outdoors daily, read the papers, and seemed perfectly comfortable. Evidently it is not the anæmia itself which kills the patient.

The lowest counts on record are that reported by Quincke—143,000 per cubic millimetre, and that of Hills[2]—155,280

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[1] Cf. Schaumann: Out of his 38 cases, 1 was over 2,000,000; 26 were between 1,000,000 and 2,000,000; 11 below 1,000,000, average 1,290,000.

[2] Hills: Boston Medical and Surgical Journal, 1898, vol. 139, p. 542.

Quincke's case later improved so much that the corpuscles rose to 1,234,000 within seventy-four days of the count of 143,000 She lived several months "fat and well nourished." Hills' case died in a few days.

Table I.

Pernicious Anæmia (139 cases).

a. *Red cells* at the first examination ranged:

From 500,000 to 1,000,000 in	36
" 1,000,000 to 1,500,000 in	55
" 1,500,000,000 to 2,000,000 in	39
Total cases under 2,000,000	130
From 2,000,000 to 2,500,000 in	9
	139

b. Leucocytes numbered (when first examined):

Under 1,000	11
1,000 to 3,000	29
3,000 to 5,000	53
5,000 to 7,000	28
7,000 to 10,000	14
10,000 to 13.000	4
	139

c. Hæmoglobin (first examination):

Relatively high in	98
Not relatively high in	41
	139

d. Average diameter of red cells at time of final examination:

Increased in	118
Not increased in	21
	139

e. Megaloblasts at time of first examination:

Predominated in.	109
Later examination, predominated in	27
Only one examination, no megaloblasts	3
	139

f. **Lymphocytes averaged between 20 per cent and 30 per cent in..**	**41**
" " " 30 " " 40 " "..	**41**
" " " 40 " " 60 " "..	**47**
" " " 60 " " 80 " ".	**7**
" " " 80 " " 90 " "..	**3**
	139

g. **Eosinophiles averaged:**

Under 4 per cent.	**116**
Over 4 per cent	**15**
None found	**8**
	139

h. **Myelocytes. Present in 86 cases. Highest percentages:**

10 per cent in	**2**
9 " "	**1**
8 " "	**2**
7 " "	**2**
	7

The great but temporary improvements above alluded to, followed by relapse, occur either with or without treatment. In the course of a few months the count of red cells may rise to normal, the nucleated corpuscles (see Charts) disappear, and the patient is apparently restored to health and goes to work with a laugh at the doctor. I have followed one case through five such relapses in a period of three years before the fatal issue came. Frequently the patient feels so well during one of these remissions that he goes to work and is lost sight of, and, under such conditions, the incautious are apt to report "cure."

The *accompanying charts*[1] show the three types usually met with; No. II. being, of course, only a fragment of a case similar to No. I., while the steady progression of No. III. may have been preceded by a rise from a former downfall, though no such history was obtained.

Looking over a considerable number of cases, one can hardly help being struck with the tendency of the count to remain near the figure 1,000,000. The red cells rarely remain stationary at, say, 2,000,000, and often death may occur without the red cells sinking below 1,000,000. It seems as if some self-applying mechanism tended to arrest the destruction of corpuscles at or near this point.

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[1] The number of perpendicular lines represents the number of weeks.

In counting the red cells some difficulty and error may result from the very small size of some of the cells. It is especially important that the diluting solution should be clean and freshly made, else without the aid of a stain it may be hard to distinguish the dwarf cells or microcytes from bits of extraneous substance.

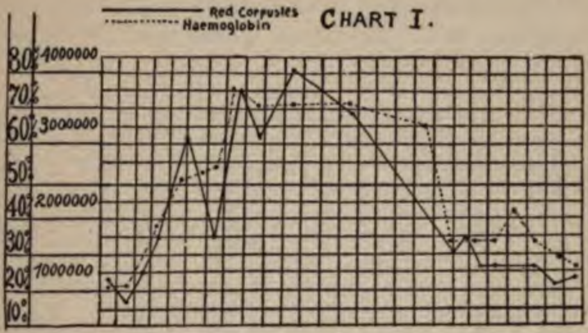
CHART I.

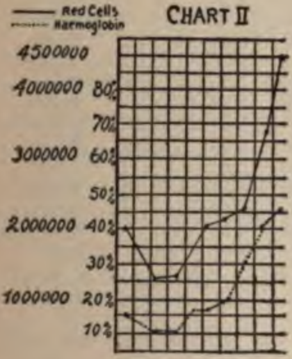
CHART II

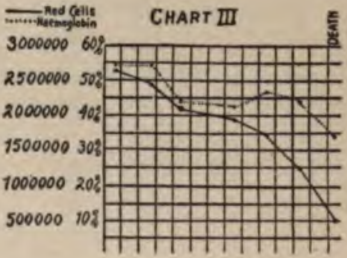
CHART III

QUANTITATIVE CHANGES.

White Corpuscles (see Table I.).—The rule is a very considerable diminution in the number of leucocytes. Thus of 139 cases which I have examined 103 were under 5,000, the average of all being about 3,800.

[I have excluded from this series counts made immediately after hemorrhage and counts in infants. The latter are very apt to show a leucocytosis in connection with *any* form of anæmia.]

As the disease progresses the leucocytes fall even more rapidly than the red cells, and counts as low as 500 white cells per cubic millimetre are not uncommon.[1]

Leucocytosis, when present in the blood of adult cases, is always due to some complication like hemorrhage or suppuration.

As mentioned above, the blood plates and fibrin are much diminished.

TABLE II.—WHITE CELLS.—FIRST EXAMINATION IN SIXTY CASES.

No.	White cells.	No.	White cells.	No.	White cells.
1	400	21	2,900	41	4,828
2	500	22	3,000	42	4,900
3	800	23	3,000	43	5,000
4	1,000	24	3,200	44	5,200
5	1,000	25	3,200	45	5,300
6	1,000	26	3,300	46	5,500
7	1,500	27	3,400	47	5,600
8	1,600	28	3,500	48	6,000
9	1,800	29	3,600	49	6,000
10	2,000	30	3,700	50	6,000
11	2,000	31	3,704	51	6,400
12	2,000	32	4,000	52	6,500
13	2,000	33	4,000	53	7,000
14	2,000	34	4,000	54	7,200
15	2,300	35	4,000	55	7,500
16	2,600	36	4,200	56	7,600
17	2,800	37	4,300	57	9,000
18	2,800	38	4,400	58	9,600
19	2,800	39	4,500	59	10,000
20	2,800	40	4,720	60	10,100
				Average	= 3,800 +

In four cases in which Dr. Lindström, of Boston, was kind enough to give massage, we were unable to see the slightest gain either in corpuscles or hæmoglobin, such as can be produced temporarily in most healthy persons. The observations of J. Mitchell on this point we were unable to confirm.

Hæmoglobin.

The great majority of cases of pernicious anæmia have a relatively high percentage of hæmoglobin (*e.g.*, 1,000,000 red cells and 35 per cent of hæmoglobin, or a color index of 1.75). Ehrlich has several times found it over 50 per cent even in the severest cases, and once as high as 65 per cent.

---

[1] Da Costa (page 227) states that in rare instances the leucocytes "appear to be entirely absent, none being found after prolonged search through the counting chamber and in the stained films" (!?).

This high color index is not, however, peculiar to this disease. It has been noted in acute leukæmia, in "splenic anæmia" (McCrae), in malaria, in hæmolysis from acetanilid, and in leprosy.

Of the 139 cases in the series on page 125, in which the hæmoglobin was tested, a color index of over 1 was apparently present in 98, or 71 per cent, and a color index of less than 1 in 41, or 29 per cent, of the cases. How many of these hæmoglobin estimations may have been wrong I cannot say.

From the frequency with which we find the corpuscles well stained and larger than normal in pernicious anæmia (see below), we should expect that the hæmoglobin *would* be relatively high, and in a larger percentage of cases than the v. Fleischl instrument indicated.

An increased color index is probably a bad prognostic sign. In the remissions of the disease, when the cells are increasing fast, the hæmoglobin lags behind and the color index is *low*. As the relapse follows, the color index in many cases progressively increases. Cases *whose color index is low* and in which the average diameter of the red cells is normal *are apt to be gaining at that time*, while those with high color index are apt to be losing at that time.

The average color index in the cases in which hæmoglobin and red cells were both tested was 1.04, the average percentage of hæmoglobin being 26 and of corpuscles 24 (= 1,200,000).

QUALITATIVE CHANGES.

1. Red Corpuscles.

We must distinguish here between

I. The active stages of the disease and

II. The remissions.

In the active stages we find:

(*a*) *Increase in the average diameter* of the cells is a very constant and striking feature of the stained specimens in this disease. In no other disease do so large cells or so many of them occur.

The average diameter may rise as high as 11 to 13 μ, but as a rule the average is reduced by the presence of a few abnormally small forms. The percentage of oversized cells gives us a better idea of the facts. Thus Ehrlich in 8 cases of pernicious anæmia found the following percentages of oversized red cells: 71, 71, 66, 65, 60, 58, 57, 56. In 5 convalescent cases 33 to 50 per cent of the cells were oversized and in the period of complete remission from 0 to 14 per cent.

Out of 139 cases in which I have looked for this point, 109 showed the increase, as far as could be judged without measuring many cells. This does not mean that every cell is larger than normal, but that the "macrocytes" are more numerous than the "microcytes." Occasionally we see cells over 20 μ in diameter, some with nuclei, some without.[1]

(*b*) *Deformities in Shape.*—The eye soon gets used to the shapes assumed by the necrobiotic corpuscles and learns to distinguish them from the distortions due to technique or to crenation. Most of them fall under one or another of the types shown in Plate IV. The very large forms are generally oval, but seldom present any further deformities. Among the smaller cells the battledore and sausage-shaped forms are very common. In one case I found all the red cells of the latter shape, so that they looked at first sight like a lot of gigantic bacilli. That this appearance was not due to the technique[2] (as I had at first supposed) is probable from the fact that the rod-shaped cells did not point all in one direction as they would have done if pulled out of shape by the process of spreading (see Fig. 27.) This appearance is only an exaggeration of what may be seen in most severe anæmias, namely, a tendency towards an oval shape like that of amphibian corpuscles. This is usually true of those cells (in pernicious cases) which are not more violently deformed. The type of cell so common in secondary anæmia—well stained at the edges and pale in the middle—is rarely seen.

Occasionally we see cases with no considerable deformities whatever in the red cells. In nine cases out of sixty in which this point was observed, little or no deformity was noted. I cannot make out that such cases have any better or worse prognosis than others. I have never seen cases whose red cells were all *undersized*, but a normal average diameter was present in somewhat under one-quarter of the cases in which I have looked out for this point.

---

[1] Capps has recently proved the increase in the size of the red cells by determining in an ingenious way what he calls the *volume index.* With the hæmatocrit he determines the volume of the red cells in a given amount of blood, and compares this figure with the count. If in a blood containing 1,000,000 red cells (one-fifth the normal), the column packed down by the hæmatocrit is more than one-fifth as long as that obtained by centrifugalizing normal blood, then the volume index is above the normal. This high volume index he finds regularly in the exacerbations of pernicious anæmia.

[2] Some writers advise the use of less heat than usual in dealing with cover-glass specimens of pernicious anæmia. I have not found this so, and heat as usual up to 150° C. and then stop.

(*c*) *Staining Properties of the Red Cells.*—The white spots or streaks described by Maragliano, Hayem, and others are very often seen in the red cells of pernicious anæmia despite good technique.

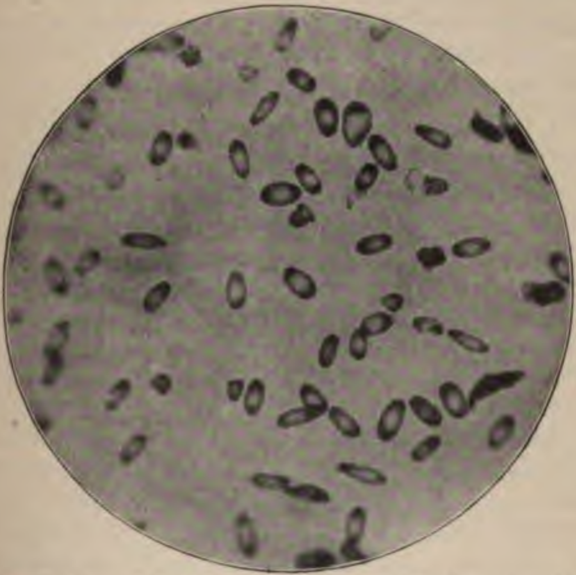

FIG. 27.—Elongated or Oval Corpuscles in a Case of Pernicious Anæmia.

Some corpuscles are so pale in the centre that we see only the narrow ring of stained protoplasm at the periphery, a mere shell. Others are swollen up so as to show no sign of central biconcavity, and stain deeply and evenly all over.

More common than in any other form of anæmia are the polychromatophilic red cells (see Plate IV.) which with the Ehrlich-Biondi mixture stain brownish, purple, or gray, either as a whole or in parts. In cover-slips stained with Wright's stain the spotted appearance of the cell, described by Ehrlich and Grawitz, is usually marked. In the nucleated red cells the protoplasm is very apt to show these changes. With Ehrlich's stain it may be difficult to distinguish normoblasts from lymphocytes. In difficult cases we have sometimes to fall back upon the appearances of the periphery, which in most red corpuscles shows some thin place or crinkle characteristic of a *flat* cell, while the lymphocyte gives us the more solid-looking outline of the *spherical* cell. With Wright's stain it is seldom difficult to make this distinction.

2. Nucleated Red Corpuscles.

Nothing further needs to be said in description of these forms (see pages 82 to 87). We have no *exact* method of estimating the number of nucleated cells either in relation to the whole number of red cells or in a cubic millimetre. All we can do is to note the number seen in *such* an area of a cover-glass specimen as is covered while counting a given number of white cells, say, 1,000. Knowing the ratio of red to white corpuscles, we can calculate from this number of nucleated red cells their approximate relation to the whole number of red cells.

Thus if the ratio of white to red be 1:1,000 (1,000,000 red and 1,000 white) and we have seen two nucleated red corpuscles while making a differential count of 1,000 white cells, the total number of red cells passed over must be approximately 1,000,000 and the number of nucleated corpuscles about 2:1,000,000 red cells or two in a cubic millimetre. Of course when leucocytosis is present and the ratio is raised—say, to 1:150 (10,000 white and 1,500,000 red) finding two nucleated red cells while counting 1,000 white would mean that there were two nucleated cells in every 150,000 non-nucleated, or twenty in a cubic millimetre (or in 1,500,000 non-nucleated cells).

Such calculations are inaccurate because we are never sure that the red cells and white cells are distributed in the dried specimen exactly as they are in the blood. Part of the leucocytes may be accumulated at the edges of the cover-glass, so that the ratio in the middle may be different from that in the circulating blood.

Nevertheless we can get some idea of how plentiful the nucleated corpuscles are, and as their significance in prognosis depends far more on their *kind* than on their *number*, greater accuracy as to the latter is not at present important. For instance, two megaloblasts per cubic millimetre mean a worse prognosis than twenty normoblasts, provided there are no other kinds present in either case. It is the *ratio* of megaloblasts to normoblasts and not the absolute number of each, that is of importance.

In all but three of the cases of pernicious anæmia in which I have examined the blood, the number of megaloblasts has exceeded the number of normoblasts, and as the cases grew worse the megaloblasts grew relatively more numerous (often absolutely as well). Further, in several hundred cases of severe secondary anæmia I have but twice seen the number of megaloblasts exceed the number of normoblasts.

The range of variation in the number of nucleated cells present has extended in my series from 6 per cubic millimetre to 7,100 per cubic millimetre (see Table III.). The calculation can be made by using the following formula:

Let n = the number of white cells counted (by differential count).
" m = " " " nucleated red cells seen while counting these.
" p = " " " white cells per cubic millimetre (Thoma-Zeiss).

$$p \times \frac{m}{n} = x = \text{number of nucleated red cells per cubic millimetre.}$$

The search for nucleated corpuscles in pernicious anæmia is sometimes the most laborious undertaking in all blood examination, but it is also one of the most important. We may search two or three hours before finding one nucleated corpuscle, but on that corpuscle may hang the character of our prognosis. If it be a megaloblast and no other nucleated red corpuscles are seen, the prognosis is bad, and it is important that we should know it. This is particularly true when the case is seen during a remission, for under these conditions we might never suspect a case of pernicious anæmia but for the presence of megaloblasts. They are not always difficult to find; indeed, in one of my cases they were more numerous than the white cells, but, as a rule, we do not get off with less than two hours' work.

The number of megaloblasts in the peripheral circulation often varies very markedly from day to day so that to-day it may be impossible to find any, while to-morrow they will be plentiful. Even in different preparations made at the same time the number of megaloblasts may vary greatly. The importance of frequent examinations is obvious in the light of these facts. Morse (*Boston Med. and Surg. Jour.*, November 27th, 1902) reports a series of cases to prove that the diagnosis of pernicious anæmia cannot be made from the blood alone, for identical blood occasionally occurs in secondary anæmias.

Case.	Diagnosis.	Red cells.	Hæmoglobin.	White cells.	Polymorpho-nuclears.	Large mono-nuclears.	Eosinophiles.	Mast cells.	Megaloblasts.	Normoblasts.	Remarks.
1.....	Malaria......	1,216,000 diam. +	?	4,200	57	36	1	6	10	1	200 counted.
2.....	Bleeding piles for 20 years.	2,208,000 diam. +	35	4,400	66	30	3	1	1	0	300 counted.
3.....	Cancer of	1,280,000	8	8,000	48	49	3	0	2	2	100 counted. May 1st.
	bladder.	1,060,000	10	7,600	..	..	..	..	2	0	100

These cases are, I think, conclusive, and two similar ones have within the past few years come to my notice and convinced me that by the blood alone the diagnosis of pernicious anæmia is not always possible. We must take account of *all* the clinical data, of which the blood is but one.

Table III. shows the number of nucleated corpuscles per cubic millimetre in thirty of the cases examined by the writer.

TABLE III.—NUMBER OF NUCLEATED RED CELLS PER CUBIC MILLIMETRE IN THIRTY CASES OF PERNICIOUS ANÆMIA.

Case Number.	Total nucleated red cells.	Megaloblasts.	Normoblasts.	Microblasts.
1................	7,100	5,300	1,325	475
2................	6,468	3,476	924	2,068
3................	854	574	266	14
4................	277	277	0	0
5................	240	160	80	
6................	229	123	106	
7................	208	130	78	
8................	200	134	66	
9................	117	103	14	
10................	116	80	36	
11................	114	95	19	
12................	112	96	16	
13................	96	96	0	
14................	96	84	12	
15................	92	59	33	
16................	46	26	20	
17................	45	36	9	
18................	39	33	6	
19................	35	32	3	
20................	28	26	2	
21................	28	21	7	
22................	28	28	0	
23................	18	12	6	
24................	14	14	0	
25................	11	11	0	
26................	11	10	1	
27................	11	9	2	
28................	9	6	3	
29................	8	7	1	
30................	3	2	1	

3. *White Corpuscles.*

Unless the cover-glasses are spread unusually thickly, it may take a long time to find enough leucocytes for an accurate differential count, so great is the leucopenia in many cases. It is worth while, therefore, to spread some of the cover-glasses more thickly than would be advisable if we had only the red cells to examine.

TABLE IV.—PERCENTAGES OF LEUCOCYTES IN PERNICIOUS ANÆMIA.

LYMPHOCYTES, LARGE AND SMALL.		EOSINOPHILES.		Number of counts.
No.	Per cent.	No.	Per cent.	
1	79.	1	9.	1
2	77.	2	6.2	1
3	71.	3	6.	1
4	61.6	4	4.7	2
5	58.	5	4.6	2
6	57.6	6	4.5	3
7	57.2	7	4.4	1
8	57.	8	4.3	1
9	56.9	9	4.	1
10	56.	10	4.	5
11	53.9	11	4.	1
12	53.8	12	3.7	2
13	51.5	13	3.5	1
14	49.5	14	3.4	2
15	49.4	15	3.4	1
16	47.9	16	3.1	1
17	47.9	17	3.	3
18	47.	18	2.8	2
19	46.	19	2.7	2
20	45.9	20	2.6	1
21	45.5	21	2.6	3
22	44.7	22	2.6	2
23	43.7	23	2.6	1
24	42.2	24	2.	1
25	41.	25	2.	1
26	40.8	26	2.	2
27	40.5	27	1.6	1
28	39.	28	1.6	1
29	38.	29	1.5	5
30	38.	30	1.5	2
31	37.8	31	1.5	1
32	36.1	32	1.5	1
33	35.7	33	1.4	1
34	35.6	34	1.2	8
35	35.6	35	1.2	1
36	34.	36	1.2	1
37	33.6	37	1.	1
38	33.1	38	1.	2
39	33.	39	1.	1
40	33.	40	.8	1

Table IV.—Percentages of Leucocytes in Pernicious Anæmia (*Continued*).

Lymphocytes, Large and Small.		Eosinophiles.		Number of counts.
No.	Per cent.	No.	Per cent.	
41	31.8	41	.8	1
42	29.4	42	.8	1
43	28.7	43	.7	1
44	28.4	44	.6	1
45	27.3	45	.5	1
46	27.2	46	?	1
47	26.5	47	.3	1
48	24.2	48	.2	2
49	22.	49	.0	1
50	21.2	50	.0	1
51	19.8	51	.0	1
52	16.	52	.0	

The essential point shown in these tables is the absolute and relative diminution in the polynuclear cells which corresponds with a percentage increase in the other forms. Absolutely the lymphocytes are about normal.

In 52 cases examined by myself the lymphocytes (large and small) averaged 45.4 per cent. About nine-tenths of these were small forms.[1] As the fatal termination approaches, the percentage of lymphocytes rises. An extreme case of this change has already been recorded on page 96; an ordinary case of pernicious anæmia developed near death a lymphocytosis of about 60,000 with 91.7 per cent of small lymphocytes.

Williamson and Martin[2] have recently recorded a similar case with the following figures:

Date.	Red.	Hæmoglobin.	White cells.	Lymphocytes.	Polymorphonuclears.	Myelocytes.
December 1	900,000	20	+	—	—	—
" 8	480,000	12	34,000	99.27	0.55	0.18
" 11	400,000	12	45,000	99.06	.56	.37
" 12	300,000	—	38,000	99.62	.37	.00
Death						

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[1] Da Costa in one-half of his cases found the large forms over 12 per cent. The average in all his cases was 10 per cent. The polynuclears averaged 58 per cent; the eosinophiles were generally decreased and in 18 per cent of the 31 cases entirely wanting. One case showed 10 per cent. of myelocytes.

[2] Williamson and Martin: Brit. Med. Journal, May 10th, 1902.

The lymphocytes were of all sizes, but faintly stained. Autopsy showed a typical case of pernicious anæmia with terminal pneumonia. No signs of leukæmic lesion in marrow or glands.

Da Costa (page 182) found eighteen hours before death that the leucocytes (which had previously numbered from 1,000 to 2,400) had risen to 18,600. The lymphocytosis was considerable—46 per cent (or 8,500 absolutely), but not extreme as in the cases above cited. Two other cases showed respectively 71 and 79 per cent of lymphocytes a few days before death. The polymorphonuclear cells suffer proportionately as a rule. On the other hand, Ewing has observed a marked rise in the percentage of the polynuclear cells near death, although autopsy revealed no complication. Pneumonia or septic complications may produce an ordinary polynuclear leucocytosis.

Eosinophiles are occasionally increased, 9 per cent being present in one of my cases, 6.6 per cent in another. The average of 78 examinations in my 52 cases is 2.7 per cent.

Small percentages of *myelocytes* are the rule. They are present in 42 of 52 cases. Table V. shows the percentages.

TABLE V.

No.	Percentage of myelocytes.	No.	Percentage of myelocytes.	No.	Percentage of myelocytes.
1	9.2	19	1.8	37	0.6
2	8.8	20	1.5	38	.6
3	8.	21	1.5	39	.5
4	6.3	22	1.5	40	.4
5	6.	23	1.4	41	.3
6	4.6	24	1.2	42	.2
7	4.	25	1.	43	.0
8	4.	26	1.	44	.0
9	3.6	27	1.	45	.0
10	3.4	28	1.	46	.0
11	3.	29	1.	47	.0
12	3.	30	.8	48	.0
13	2.7	31	.8	49	.0
14	2.5	32	.8	50	.0
15	2.2	33	.6	51	.0
16	2.2	34	.6	52	.0
17	2.2	35	.6	Average = 2 per cent.	
18	2.0	36	.6		

With a leucopenia such as is usually present in pernicious anæmia, 2 per cent of myelocytes means absolutely a very small number per cubic millimetre.

Taking 3,800 leucocytes per cubic millimetre as the average for pernicious anæmia (see page 127), 2 per cent of myelocytes amounts to only 76 per cubic millimetre. In leukæmia the absolute number of myelocytes is seldom under 150,000 per cubic millimetre.

In many cases the polynuclear leucocytes show various abnormalities in size and staining reactions. They are often smaller than normal, a peculiarity also to be noted in myelogenous leukæmia.

The Blood in Remissions.

1. The Color Index. When the red corpuscles begin to increase the color index may remain relatively high or even become still higher (Laache, Schaumann); but in the majority of cases this is not so. As a rule, in the remissions of the disease the hæmoglobin is relatively low, as in ordinary symptomatic anæmia, and I have seen two cases which, if examined for the first time during the period of remission, would have certainly been mistaken for ordinary chlorosis.

2. The Leucocytes. Coinciding with the increase in the red cells there is usually a still greater increase in the leucocytes, so that for a time a moderate leucocytosis may be present. This increase is made up very largely of polymorphonuclear neutrophiles, and is due, no doubt, to the increased activity of the marrow through which both red corpuscles and granular leucocytes are multiplied. The eosinophiles may also be increased as in the following case of Ehrlich: Red cells, 4,115,000; white cells, 18,300. Differential count of 400 cells showed: Polynuclears, 78.2 per cent; lymphocytes, 12 per cent; large mononuclears, 0; eosinophiles, 9.5 per cent. In another similar case he found 11 per cent of eosinophiles.

As the percentage of polymorphonuclear neutrophiles increases the percentage of lymphocytes decreases, and the myelocytes, which are usually present in small percentages during the active stages of the disease, disappear. The number of megaloblasts steadily decreases, and in their place normoblasts appear for a time; later they, too, leave the circulating blood. The size of the individual red cells is sometimes greater during a remission of the disease than at any other time. In one remarkable case the patient, whose symptoms had totally disappeared and who was actively at work as a newspaper correspondent, dropped in to see me one day, apparently in splendid health and spirits. His skin and mucous membranes were ruddy red, his hæmoglobin 90 per cent, yet to my great surprise I found only 2,500,000 red cells to the cubic millimetre. The stained specimens showed the largest red cells which I have ever seen, for the most part perfectly well shaped and natural looking, but averaging 12 μ in diameter. This stage is, however, a comparatively short one, and the size of the red corpuscles soon becomes normal or subnormal. The abnormal staining reactions and the oval forms disappear. As a rule, the count of corpuscles does not remain long above 4,000,000, but ranges in the neighborhood of 3,000,000 during the greater part of the remission.

3. THE RED CELLS. Usually the proportion of large forms diminishes as in Ehrlich's case: (*a*) Active stage; red cells 1,340,000, large forms 66 per cent. (*b*) Remission; red cells 4,115,000, large forms 33 per cent At the beginning of the remission the number of megaloblasts diminishes, while the normoblasts increase. Later the latter also disappear. Deformities become less marked and the achromic cells (pale centres) appear, giving the blood the appearance of secondary anæmia. Polychromatophilic and spotted cells grow less numerous, but Ehrlich maintains that the latter may remain even when the blood has otherwise regained its normal appearance. He therefore considers "spotted red cells" of value for diagnosis during remissions.

The rate of regeneration is often astonishingly rapid.

In Case VII. of my series the red cells increased from 1,800,000 to 5,200,000 in fourteen days. In Case XXXIX. the red cells increased from 2,200,000 to 4,000,000 in thirteen days. In Case LVIII. the red cells increased from 1,500,000 to 3,200,000 in twelve days. In Case XCI. the red cells increased from 1,700,000 to 3,000,000 in fourteen days.

Similar observations have been reported by Ehrlich and other observers.

It is quite possible, although I have no figures to prove it, that in the periods of decline the red corpuscles may fall as rapidly as they subsequently rise. This possibility is suggested by the fact that one rarely sees pernicious anæmia in an early stage—that is, until the red corpuscles have fallen below 2,000,000 per cubic millimetre. Only four of my cases showed more than 2,000,000 red corpuscles per cubic millimetre at the time of the first examination of the blood.

Summary.

The more important characteristics of the blood of pernicious anæmia are as follows:

1. *Red cells about 1,200,000 per cubic millimetre.*
2. *White cells much diminished,*
3. Hæmoglobin variable, *sometimes increased* relatively (= high color index).
4. Deformities in size and shape of red cells in many cases.
5. *Increase in average diameter of red cells.*
6. Polychromatophilic red cells.
7. *Megaloblasts more numerous than normoblasts.*
8. Lymphocytosis.
9. Small percentage of myelocytes.

The items italicized are the most important and characteristic.

Diagnostic Value.

1. *Pernicious anæmia and chlorosis* may be indistinguishable without the examination of the blood. The pallor of the two diseases is not always different either in degree or in kind, and the symptoms and physical signs may be identical.

The differential diagnosis is easily made by the blood. The red cells rarely reach as low as 2,000,000 in chlorosis and the number and degree of degenerative changes are less than in pernicious anæmia. Megaloblasts have been seen in chlorosis (Hammerschlag), but have never constituted a majority of the nucleated red cells present. In the great majority of cases the pallor and other signs and symptoms of chlorosis are due to lack of hæmoglobin per corpuscle (for the corpuscles are not only pale but very small-sized), and not to a lack of corpuscles. The high color index and large size of the scanty cells in pernicious anæmia contrast strongly with this.

The white cells are about the same in both diseases, though usually fewer in pernicious anæmia. Lymphocytosis is common to both diseases. Myelocytes are occasionally found in chlorosis, but much less commonly than in pernicious anæmia.

2. *Pernicious Anæmia and the Anæmia of Malignant Disease.*—Not long ago I examined the blood of a gentleman who had gradually and without assignable cause acquired a "lemon-yellow" pallor, without loss of flesh, vomiting, pain, or any localizing sign or symptom. The diagnosis of pernicious anæmia had been made.

To my great surprise I found over 4,000,000 red cells, with only 38 per cent of hæmoglobin, and 18,780 white cells, 86 per cent of which were polymorphonuclear neutrophiles. One normoblast was seen. Fibrin was not increased. The anæmia was evidently secondary, and the autopsy ten months later showed cancer of the stomach.

Osler and McCrae record a case in which the symptoms and signs (except the blood) were so suggestive of pernicious anæmia that Osler made that diagnosis. Six months later a nodular mass was felt in the region of the stomach, and the patient soon after died. In this case the red cells varied between 2,840,000 and 3,048,000. The leucocytes numbered 11,500; there were no nucleated red cells and but slight poikilocytosis. Hæmoglobin was 25 per cent, *i.e.*, the blood of secondary anæmia. I have since had four similar cases.

Malignant disease may bring down the count of red cells to 1,000,000 or lower, but *in such cases* leucocytosis is often present. As will be seen in the chapter on malignant disease, leucocytosis is by no means invariable in the anæmia of cancerous growth, but *in those cases* which cause such an anæmia as to resemble the counts of pernicious anæmia, leucocytosis is the rule. This in itself is usually sufficient to exclude uncomplicated pernicious anæmia. When an increase in the whole number of leucocytes is not present in malignant disease, there is often an increased percentage of polymorphonuclear cells, contrasting strongly with the increased percentage of lymphocytes in pernicious anæmia. Nevertheless, it is true that the blood of cases of cancer does occasionally simulate for a time that of pernicious anæmia so closely that, *judging from the blood alone*, the two diseases are indistinguishable. The other clinical data must be kept in mind.

Normoblasts and not megaloblasts are the rule in malignant disease. If megaloblasts are present they are almost always in the minority, while in pernicious anæmia they are in the majority. The average size and staining power of the red cells is increased in most cases of pernicious anæmia and decreased in most cases of malignant disease.

Ehrlich has twice diagnosed pernicious anæmia from the blood examination and been confronted at the autopsy with small cancerous growths in the stomach. In one case the cancer was "the size of a hazelnut"; in the other, "an annular fibrous cancer of the pylorus without any ulceration." In these cases I believe the cancer to have been a complication and not the cause of the anæmia. Such small growths are very rarely associated with any anæmia at all.

Hayem insists that pernicious anæmia may be distinguished from anæmia secondary to cancer, because in cancer the clot contracts firmly and squeezes out the serum, and the blood plates are but slightly diminished, while in pernicious anæmia the clot does not retract and blood plates are greatly decreased.

3. *Pernicious Anæmia and Other Secondary Anæmias.*—Most secondary anæmias which are severe enough to reduce the count of red cells below 2,000,000 follow the type of malignant disease and show leucocytosis. The great pallor and dyspnœa seen in connection with some cases of *tuberculosis* and *nephritis* rarely mean a low count of red cells, but simply a loss of hæmoglobin. I remember two cases in adjacent beds at the Massachusetts General Hospital, both with extreme yellow pallor without emaciation; one had 1,020,000 and the other 4,100,000 red cells, the hæmoglobin in each being about thirty per cent. The first was pernicious anæmia, the second nephritis.

Chronic bleeding from internal piles is sometimes quite unknown to the patient, and so leads to an extreme anæmia, which is not unfrequently mistaken for pernicious anæmia. Cases of the kind have been observed by Ewart (*Therap. der Gegenwart*, November, 1899), by T. R. Brown, and by myself. In details, however, the blood is quite unlike that of pernicious anæmia.

Purpura, typhoid, lead poisoning, chronic malaria, and other diseases may reduce the red cells to a point as low as that seen in early stages of pernicious anæmia and may *not be accompanied by leucocytosis;* but the absence of changes most characteristic of the latter disease (a majority of megaloblasts, increased diameter and color index in the red cells) serves in most cases to make the diagnosis clear.[1] Nevertheless, I have been recently convinced that the blood of cases of secondary anæmia may exceptionally present appearances indistinguishable from that of pernicious anæmia (see page 134). Cases involving hæmolysis (poisoning by acetanilid, nitrobenzol, etc.) may also be associated with blood changes like those of pernicious anæmia, and the bothriocephalus anæmias, which show all the blood changes just described, must surely be classed as *secondary*.

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[1] Another point of difference emphasized by Grawitz is that the plasma of pernicious anæmia has a relatively larger amount of solids than that of anæmia secondary to the above diseases. This is hardly a clinically applicable test, but is said to be a valuable one.

It appears, therefore, that the blood alone is not always sufficient for the diagnosis of pernicious anæmia. This is especially true during the remissions of the disease, but even in its active stages the disease produces changes which are occasionally reproduced in all particulars by cases of anæmia whose cause is obvious, especially by those involving hæmolysis. The blood of pernicious anæmia appears to be the result of one type of chronic hæmolysis.

4. *Pernicious Anæmia and Leukæmia.*—Occasionally in infants these two diseases seem to approach very near each other and are difficult to distinguish. In infancy, as is well known, any anæmia (primary or secondary) is apt to be accompanied by leucocytosis and an enlarged spleen. Further, leukæmia, which in adults usually causes a relatively slight anæmia, affects the red cells much more strongly in infancy, and may reduce them to a number decidedly suggestive of pernicious anæmia. Therefore in both diseases we may have enlarged spleen, great anæmia, and leucocytosis.

The one characteristic point of leukæmic blood—the abundance of myelocytes—usually enables us to distinguish the two diseases, for although present in both diseases the myelocyte is much more plentiful in leukæmia. Unfortunately we have no way of fixing just *how* numerous myelocytes must be in order to constitute leukæmia. It is only in infancy, and very rarely then, that this difficulty arises, but at that period I am inclined to believe that we sometimes see conditions intermediate between the two diseases, indicating the ultimate identity of the two. Their numerous clinical resemblances cannot here be discussed. (For further comment on this point see page 525.)

Prognostic Value of Blood in Pernicious Anæmia.

The prognosis is always very bad, but the following scheme indicates the presence of a severe or of a mild type:

1. *Severe* (*rapidly fatal*).	2. *Less Severe* (*slower course*).
(*a*) Extreme progressive anæmia.	(*a*) Remissions.
(*b*) High color index.	(*b*) Normal or low color index.

(*c*) Increase in size of red cells.	(*c*) Normal-sized or small cells.
(*d*) Degenerative changes.	(*d*) No degenerative change.
(*e*) Numerous megaloblasts.	(*e*) Numerous normoblasts.
(*f*) Few or no normoblasts.	(*f*) Few megaloblasts.
(*g*) Lymphocytosis.	(*g*) Normal percentage of polymorphonuclear cells.

It has been thought by some observers that the absence or great scantiness of nucleated corpuscles indicated lack of any effort at regeneration on the part of the blood-making functions, and hence a peculiarly malignant type of the disease. I have never seen cases

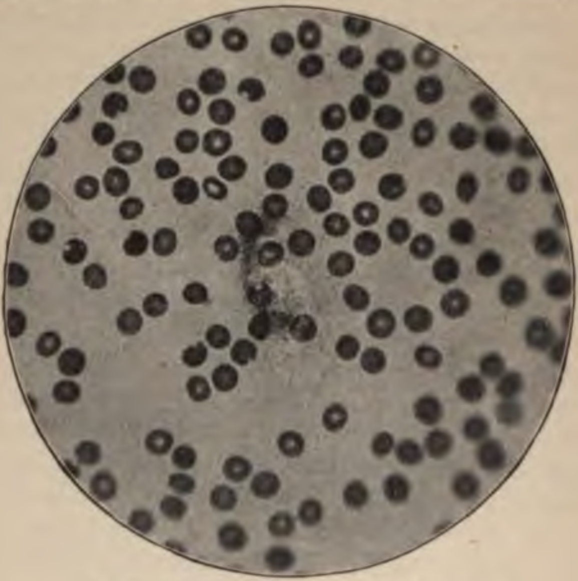

FIG. 28.—Normal Blood. Magnified 350 diameters.

	Pernicious anæmia.	Chlorosis.	Secondary anæmia.
Red cells	About 1,000,000	Rarely under 2,000,000	May be 1,000,000 or less.
White cells	Usually decreased	Usually normal	Usually increased.
Hæmoglobin	Often relatively high	Always relatively low	Relatively low.
Megaloblasts	Constitute the majority of the nucleated red cells.	Rare	Rare; never more numerous than normoblasts.
Normoblasts	Less numerous than the megaloblasts.	Occasional; always more numerous than megaloblasts.	Common.
Size of red cells	Increased	Diminished	Various; not increased.
Lymphocytes	Increased	Increased	Usually diminished.
Polymorphonuclear cells.	Decreased	Decreased	Usually increased.
Myelocytes	Common	Rare	Rare.

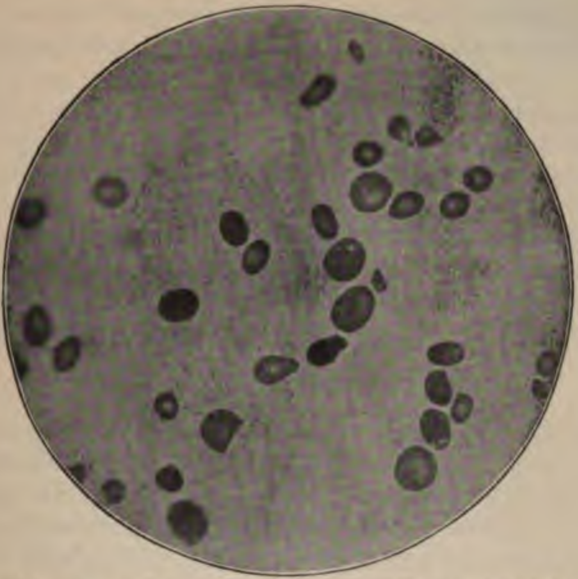

FIG. 29.—Pernicious Anæmia. Magnified 350 diameters. Note the relatively large size and well-stained centres of the cells.

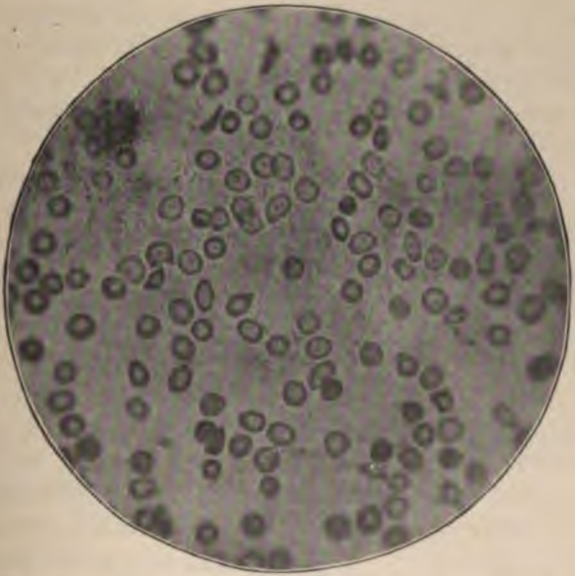

FIG. 30.—Chlorosis. Magnified 350 diameters. Note small size and pale centres.

in which nucleated corpuscles were steadily absent, but their scantiness has seemed to me as a rule to be associated with a more *slowly* fatal type of the disease.

No significance has seemed to me to attach to the presence of larger or smaller percentages of eosinophiles.

To illustrate the different size of the cells in chlorosis and pernicious anæmia I have had photographs taken of the blood of a case of two of these diseases and of normal blood, *all on precisely the same scale* (see Figs. 28, 29, 30).

2. FATAL ANÆMIA WITH HYPOPLASTIC MARROW.

("*Aplastic Anæmia.*")

Ehrlich reported in 1888[1] the case of a girl of twenty-one with cutaneous, uterine, buccal, and retinal hemorrhages, which caused death within thirty days from the first symptom. Blood examination showed 213,360 red cells—small, fairly stained forms predominating. Deformities were slight. No nucleated red cells could be found despite many hours' search before and after death. Leucocytes numbered 200 per cubic millimetre—an astonishing leucopenia. Eighty per cent of these white cells were lymphocytes and 6 per cent large mononuclears, leaving but 14 per cent (or 28 per cubic millimetre) of polynuclear neutrophilic cells. In other words, the neutrophiles were reduced to about $\frac{1}{170}$ of their normal number, while the lymphocytes were distinctly though less markedly diminished. Eosinophiles were wanting altogether.

The great diminution in red cells and granular leucocytes in this case suggested to Ehrlich a lack of compensatory reaction on the part of the marrow. Autopsy confirmed this. The marrow of the femur was yellow throughout except for a tinge of red near one end.

Similar cases have lately been reported by Lipowski,[2] Muir,[3] and others. In these, as in Ehrlich's case, hemorrhages were prominent.

The red cells in Muir's case were normal in size and their number was reduced to 800,000 and the hæmoglobin to 11 per cent. The leucocytes numbered 7,000 per cubic millimetre, but only 25 per cent of them were polynuclear neutrophiles. Eosinophiles and blood plates were entirely absent. No nucleated red cells could be found in the blood, and only one or two in the marrow, post mortem, despite long and careful search. The marrow was of the fatty type, almost white, and contained few neutrophiles and *no eosinophiles.*

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[1] Charité-Annalen, xiii.

[2] Lipowski: Deut. med. Woch., 1900, p. 340.

[3] Muir: Brit. Med. Jour., 1900, p. 910.

In Lipowski's case, as in Ehrlich's and in Muir's, the disease was dubbed "purpura hæmorrhagica" owing to the profuse hemorrhages from mucous, serous, and cutaneous surfaces. The red cells were 2,112,000, hæmoglobin was 18 per cent. Only 7 per cent of the leucocytes were neutrophiles, the rest lymphocytes. Nucleated red cells were absent.

3. THE BLOOD IN CHLOROSIS.

This has been already described for the most part under the heading of Secondary Anæmia. In many cases the two are indistinguishable by the blood examination alone, the changes consisting simply in the presence of light, small-sized, pale, more or less deformed red cells whose number may or may not be decreased, according to the severity of the case. Leucocytosis is rarely if ever present in uncomplicated chlorosis, but is often absent in secondary anæmia. Normoblasts may be present in both. The chief points of distinction are:

(*a*) The red cells are more apt to be uniformly under-sized and under-colored in chlorosis, while in secondary anæmia we more often find normal cells among the diseased ones.

(*b*) The color index may be lower in chlorosis than is common in secondary anæmia, and this lowering is more constant in chlorosis.

(*c*) Absolute diminution in the number of polynuclear leucocytes, which is very common in chlorosis, is not so common in secondary anæmia.

(*d*) Nucleated corpuscles are less common in chlorosis than in anæmia secondary to malignant disease.

(*e*) Coagulation is rapid, in contrast with the very slow clotting of pernicious anæmia and of many secondary anæmias. Yet fibrin is not increased. The increased rate of coagulation seems to be connected with the marked increase in blood plates, which is almost always present.

Volume and Oxygen Capacity of the Blood.

The blood volume is greatly increased. In 21 cases with hæmoglobin below 50 per cent Smith found the average volume 4,883 c.c., or over one-half greater than the normal average (3,240). The volume is increased in proportion to the severity of the disease. Some cases showed 6,400 c.c. of blood, or nearly double the average. At the same time the total oxygen capacity (or total hæmoglobin) is approximately normal, averaging over 95 per cent in 21 cases. As the specific gravity of the plasma is normal, there appears to be a great increase in the amount of normal plasma. If we were to imagine this excess of plasma filtered off, there would remain (*e.g.*, in Case X. of Smith's series with 6,266 c.c. and 2,600,000 red cells) about 8,000,000 red cells per cubic millimetre. Hence Smith concludes that there is really a large absolute increase in the number of red and white cells disguised by an excess of plasma. Under treatment the oxygen capacity or hæmoglobin is not *really* increased, but the amount of plasma diminishes—in one case from 4,574 c.c. to 2,800 c.c.

The Blood in Gross.

The pallor of the drop is sometimes excessive, fully as great as in pernicious anæmia; the liquid is very fluid and thin, and flows abundantly on puncturing the skin. Yet it coagulates very rapidly and our technique must be prompt.

RED CELLS AND HÆMOGLOBIN.

Quantitative Changes.

Hayem has recorded cases whose count was as low as 1,662,000 and even 937,360 per cubic millimetre. Such figures are certainly rare in this country, and the striking fact is usually the *slight* numerical loss of red cells, considering the extreme pallor of the patients.

The lowest count in the Massachusetts General Hospital series was 1,932,000, in W. S. Thayer's 63 cases 1,953,000, and in Da Costa's 1,720,000. The accompanying tables, from the records, show the range of red cells and hæmoglobin in 192 cases as counted when the patients first came under observation. The highest counts (7,100,000 and 5,884,000) are undoubtedly due to some temporary stasis or concentration of the blood.

The average of the 192 cases, 4,052,000 red cells per cubic millimetre, is about the same as in Thayer's[1] series, the average of which is 4,096,544, while Da Costa's average in 106 cases is 3,876,000.

The average hæmoglobin percentage of this series, 40.4 per cent, is also very close to Thayer's (42.3 per cent) and to Da Costa's (41.3 per cent). This gives us a reduction of the corpuscle substance to one-half the normal, or to the equivalent of 2,250,000 healthy red cells; 101 of the 192 cases have 4,000,000 or more red cells. These figures do not agree with those collected by v. Limbeck, in which only 99 out of 247 are over 4,000,000. But this probably means simply that in this country the patients seek medical advice before their disease has advanced very far, while in Germany they wait longer before resorting to a hospital. For, as above explained, in all anæmias the individual corpuscles suffer in quality first and only after some time begin to decline in number. This is especially the case in chlorosis, although by no means peculiar to that disease.

The color index is invariably low, as seen in the table, although it is rare to see it fall below 0.30. In only four cases of the present series did it go below that figure, the average being about 0.50.

v. Noorden[2] found that the color index was especially apt to be low in first attacks and less often in the recurrent or habitual cases, but Romberg,[3] in a study of one hundred and seventeen cases, has not found this true, and I agree with Romberg. One of the lowest color indexes in my series was in a woman over fifty who had a truly habitual chlorosis.

TABLE VI.—CHLOROSIS.

Red Cells.	Cases
Between 7,000,000 and 8,000,000	1
" 6,000,000 " 7,000,000	2
" 5,000,000 " 6,000,000	26
" 4,000,000 " 5,000,000	72
" 3,000,000 " 4,000,000	64
" 2,000,000 " 3,000,000	26
" 1,000,000 " 2,000,000	1

Average of these 192 cases = 4,052,000

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[1] See Osler's article on Chlorosis in the "American Text-Book of Medicine," vol. ii., 1894.

[2] "Chlorosis," Wien, 1897 (Hölder).

[3] Berl. klin. Woch., June 28th, 1897.

White cells.	Cases.
26,000	1
Between 15,000 and 14,000	4
“ 14,000 “ 13,000	3
“ 13,000 “ 12,000	9
“ 12,000 “ 11,000	13
“ 11,000 “ 10,000	15
“ 10,000 “ 9,000	12
“ 9,000 “ 8,000	10
“ 8,000 “ 7,000	34
Between 7,000 and 6,000	30
“ 6,000 “ 5,000	20
“ 5,000 “ 4,000	17
“ 4,000 “ 3,000	10
“ 3,000 “ 2,000	2
“ 2,000 “ 1,000	2
	182
Average, 7,810	

PER CENT OF HÆMOGLOBIN IN CHLOROSIS.

Between 10 and 19 = 9 cases.
“ 20 “ 29 = 36 “
“ 30 “ 39 = 52 “
“ 40 “ 49 = 40 “
“ 50 “ 59 = 41 “
“ 60 “ 69 = 16 “
“ 70 “ 80 = 3 “

197 “
Average, 40.4 per cent.

The striking contrast is with pernicious anæmia, rather than with secondary anæmia. In the former the color index, as above mentioned, averaged 1.04 in 68 cases. In secondary anæmia it is almost always below 1, but does not *average* so low as in chlorosis, although in individual cases it may be very low.

For example, Osterspey quotes a case of gastric cancer with a blood count of 4,230,000 red cells, and only 22 per cent of hæmoglobin, a color index of 0.26.

Qualitative Changes.

(*a*) The stained specimen shows a greater or less degree of *pallor of the corpuscle centres* corresponding so accurately to the diminution in hæmoglobin that a practised observer can tell approximately how low it is simply from the stained specimen. The pallor, however, is to be taken in connection with the *size* of the cells, for the diminution in hæmoglobin is not due simply to a bleaching out of the cells, but to their loss of size. Hence,

(*b*) *The diminution in the average diameter* of the cells is a very important feature. In the convalescent we may watch the gradual increase in the average diameter of the cells from 5.5 μ or lower up to 7.9 μ or even 8.2 μ in many cases. Both in this respect and as regards the bleaching of individual cells, many cases contrast with most secondary anæmias, in that a large proportion of the cells are affected alike, *i.e.*, are small and pale, while in secondary anæmia there are apt to be well-stained and good-sized or over-sized cells in every field. These last occur also in chlorosis, but less frequently as a rule. Hence the usually lower color index of chlorosis. In certain cases this distinction does not hold, and the two conditions are identical in so far as the size and color of the red cells are concerned.

(*c*) *Deformities in size and shape* are very common in all advanced cases, but often absent in mild or moderate ones. They present no special peculiarities except that macrocytes are relatively rare and microcytes relatively common. In the severest cases, however, the macrocytes begin to get more numerous and we approach the picture of pernicious anæmia.

(*d*) *Changes in Staining Reaction.*—Polychromatophilia, basophilic red cells, or stippling is rare, but, despite Grawitz's statement, may be occasionally seen in severe cases.

(*e*) *Nucleated red corpuscles* are *very* scanty even in advanced cases. Most observers find them in small numbers after long search. They are almost always of the normoblast type, but megaloblasts have also been found. In four cases of my series normoblasts in small numbers have been found—never more than one hundred and twelve per cubic millimetre. I have never found megaloblasts.

The scantiness of nucleated red cells is a point of contrast with the anæmia secondary to malignant disease, in which even in mildly anæmic states we readily find nucleated corpuscles, while in chlorosis, even in severe cases, a long search may show very few or even none at all.

Specific Gravity.

Chlorosis is usually agreed to be one of the diseases in which specific gravity and hæmoglobin run parallel, and as the inaccuracies and inconveniences of the v. Fleischl instrument are so great, it seems to the writer better to follow the specific gravity rather than the hæmoglobin. The tables on page 39 (Part I.) show how the inference from density to coloring matter can be made. A specific gravity of 1030 is not very rare.

WHITE CELLS.

A. Quantitative Changes.

Leucocytosis is absent in uncomplicated cases. In the series in Table VI. the occasional leucocytosis may be due to digestive or to a variety of other influences (uterine troubles, etc.), which could not be excluded.

The average in Thayer's 63 cases was 8,467 and in Da Costa's 7,090; in the present series it is just under 8,000.

As in pernicious anæmia, the worst cases are apt to have leucopenia, and as improvement progresses the white rise even faster than the red corpuscles. Thus in Romberg's careful study of 117 cases, 24 cases whose hæmoglobin was under 40 per cent had an average of 6,350 leucocytes per cubic millimetre, while 52 cases whose hæmoglobin averaged 60 per cent had an average of 9,250 leucocytes. We found the average in healthy girls of the same age to be 9,068 white cells per cubic millimetre.

The absence of leucocytosis is the most important point in distinguishing chlorosis from secondary anæmia due to cancer, suppuration, etc.

B. Qualitative Changes.

Lymphocytosis is usually present, as in pernicious anæmia, whenever the disease is well marked, and sometimes even in mild cases. Thus Rieder found in 12 cases an average of 33 per cent of lymphocytes, the highest percentages being 53.7, 43.5, and 41.7; but Da Costa in 37 cases found rather low figures for the small lymphocytes. In his series eosinophiles were notably decreased, and in 70 per cent of his cases entirely absent. Either the small or the large lymphocytes may predominate. In my own experience it has usually been the small forms, while Da Costa has found an average of 15.5 per cent of large mononuclear forms (including large lymphocytes) in his 37 cases. In one case he made out 40 per cent of these cells with only 32 per cent of polymorphonuclear.

The neutrophiles suffer proportionally, their low percentage contrasting often with that of secondary anæmia associated with leucocytosis. Eosinophiles are occasionally increased. In Rieder's 12 cases the average percentage was 3.5, the highest percentages being 9.6 and 7 per cent.

Myelocytes are rare but have occasionally been observed in small numbers.

Regeneration of the Blood.

As the patients begin to mend under the influence of treatment, the blood changes are just the reverse of those seen during the development of the disease. First the corpuscles gain in numbers, the hæmoglobin still remaining low; later and much more slowly the coloring matter, size, and weight of the cells are renewed. It seems as if the new-formed cells were of light weight and had to be replaced gradually by cells of normal stature. The nucleated corpuscles and deformities disappear and the leucocytes shoot up often a little above the normal.

Blood Plates.

They are considerably increased.

Chlorosis without Known Blood Changes.

Romberg quotes the following facts: Three girls, nineteen, twenty, and twenty-five years of age, came to him with typical symptoms of chlorosis. Their blood counts showed:

I. Red cells, 5,246,000 ; Hb. 80 per cent.
II. " " 5,376,000 ; " 83 "
III. " " 4,408,000 ; " 87 "

All improved markedly under iron treatment.

I mention this because I have seen several similar cases and have heard of others from colleagues.

Summary.

1. Blood as a whole: Very pale in marked cases, very fluid, but coagulates rapidly. Fibrin not increased. Specific gravity usually low, running parallel with the hæmoglobin.

2. Red cells: Average 4,000,000 when the patient is first seen, very rarely go below 1,000,000. The majority of them are *small-sized, pale*, often deformed. Nucleated corpuscles are rare (normoblasts as a rule).

3. White cells not increased.

Lymphocytosis, occasionally eosinophilia.

4. Blood plates increased.

Diagnostic Value.

1. The points of difference from pernicious anæmia have been discussed (see page 140).

2. It is important to distinguish it from simple debility, and from cases in which the skin only is anæmic; in both of these conditions the blood is normal.

3. From secondary anæmia it may be indistinguishable in case the latter be without leucocytosis. When leucocytosis is constantly present and the percentage of polymorphonuclear leucocytes is increased, chlorosis (uncomplicated) can be excluded. Of course many of the complications which may occur in chlorosis are accompanied by leucocytosis.

CHAPTER II.

LEUKÆMIA.

THE distinction between leukæmia and leucocytosis has been sufficiently dwelt on above.

The blood of the vast majority of cases of leukæmia falls clearly under one or the other of two distinct types, *myeloid* on the one hand, *lymphoid* on the other. Myeloid blood is found only in cases with great hypertrophy of the spleen, marked marrow changes, and little or no enlargement of the other lymphatic tissue. Such cases are usually chronic (two to five years).[1] Lymphoid blood, on the other hand, may be associated either with acute or chronic forms of the disease, the lymphatic glands may or may not be enlarged, and the spleen may be as big as in cases of the myeloid type. The diagnosis of leukæmia can easily be made by the blood alone, but we cannot say from the blood whether or not the spleen or the visible lymph glands are hypertrophied. In acute lymphæmia the lymph glands of the alimentary tract (cervical, faucial, gastro-enteric, mesenteric) may be the only set involved, or the process may not involve the lymphatic glands at all. At least nine cases of this type have been reported, all of them acute and apparently originating like the "myeloid" cases from the marrow itself. The matter has been discussed and studied, especially by Walz,[2] by Pappenheim,[3] and by Dorothy Reed.[4]

All of the forty-nine cases associated with myeloid blood which have come under my observation have run a chronic course, while of the cases showing lymphæmia seven were chronic, five acute, and five subacute. All the myeloid cases had very large spleens without enlargement of visible lymph glands, but three of the lymphatic cases had spleens almost filling the abdomen.

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[1] But Grawitz (p. 333) and Reimann (Wien. klin. Woch., 1899, No. 39) have reported cases which appeared to be acute.

[2] Walz: Centralb. f. allg. Path., 1901, p. 967.

[3] Pappenheim: Virchow's Archiv, vols. clvii., clix., and clxvi.

[4] Dorothy Reed: Am. Jour. Med. Sc., October, 1902. See also Kelly: Trans. Assn. American Phys., 1903.

The disease leukæmia, then, is associated with two types of blood.

1. Myeloid blood.
2. Lymphoid blood.

I. MYELOID LEUKÆMIA.

The drop as it emerges from the puncture looks somewhat opaque in color, but is neither whitish nor chocolate-colored. It flows very sluggishly, however, and is difficult to spread between cover-glasses owing to the masses of white cells contained in it.[1] Coagulation is normal, three minutes or less with Wright's coagulometer, and fibrin is not increased.

Red Cells.

In the earlier stages of the disease there is no anæmia. Later the diminution in red cells is moderate, averaging about 3,120,000 in the forty-seven cases of Table VII. Toward the end of life the count of red cells often falls below 2,000,000. The patients are *often not pale* and may feel perfectly well. The hæmoglobin is usually diminished, the color index being about 0.6 in my cases. It is difficult to read the v. Fleischl instrument in leukæmia, as the presence of so many leucocytes gives a muddy tint to the liquid, not easy to compare with the red of the glass.

Table VII.—Leukæmia.

No.		Red Cells.	No.		White Cells.
1	Highest.	5,000,000	1	Highest.	1,072,222
2		4,877,000	2		980,000
3		4,800,000	3		820,000
4		4,592,000	4		800,000
5		4,288,000	5		756,000
6		4,140,000	6		748,000
7		4,016,000	7		716,000
8		3,832,000	8		656,000
9		3,760,000	9		626,600
10		3,635,570	10		570,000
11		3,605,000	11		500,000
12		3,584,000	12		492,000
13		3,572,000	13		454,000

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[1] Hence use a very small drop and warm the cover-glasses at the last moment before the blood touches them.

TABLE VII.—LEUKÆMIA (*Continued*).

No.		Red Cells.	No.		White Cells.
14		3,400,000	14		453,000
15		3,292,000	15		448,000
16		3,232,000	16		448,000
17		3,200,000	17		430,000
18		3,170,000	18		428,000
19		3,090,000	19		420,000
20		3,080,000	20		405,000
21		3,020,000	21		400,000
22		3,078,000	22		394,000
23		3,010,000	23		386,000
24		2,996,000	24		367,000
25		2,960,000	25		340,000
26		2,952,000	26		324,000
27		2,938,000	27		320,000
28		2,921,600	28		290,000
29		2,868,000	29		290,000
30		2,792,000	30		274,000
31		2,738,000	31		260,000
32		2,715,000	32		260,000
33		2,706,000	33		248,000
34		2,628,000	34		236,000
35		2,576,000	35		220,500
36		2,520,000	36		213,000
37		2,500,000	37		188,000
38		2,322,222	38		186,000
39		2,320,000	39		183,000
40		2,256,000	40		175,800
41		2,140,000	41		170,000
42		2,112,000	42		160,480
43		2,060,000	43		141,000
44		2,016,000	44		139,600
45		2,010,000	45		138,000
46		1,866,664	46		134,400
47		1,756,000	47		132,000
48		1,420,000	48		111,000
49		1,386,000	49	Lowest.	98,000
50		1,358,000		Average =	385,808
51		1,200,000			
52	Lowest.	408,000			
	Average =	2,706,039+			

Qualitative Changes.

The striking point is the presence of *very numerous nucleated red cells*, even in the absence of *any sign of anæmia*. With over 4,000,000 well-formed and well-colored red cells, we may have hundreds of erythroblasts in every cover-glass. They are as numerous in this form of leukæmia as in the worst forms of pernicious anæmia, even though the patient may be feeling nearly well. In Taylor's cases there were ten with 10,000 or less of the nucleated red cells per cubic millimetre, three with 10,000 to 20,000, and two between 60,000 and 70,000. One showed only 360 per cubic millimetre.

Both normoblasts and megaloblasts may be seen, but in most cases the latter are in the minority. In nine cases studied by Da Costa the normoblasts averaged 4,654 per cubic millimetre and the megaloblasts 1,257. Many of the normoblasts show fragmentation in their nuclei, and occasionaly true karyokinetic figures are seen. In the anæmic cases we find all the other changes in the red cells characteristic of anæmia, but the nucleated cells are almost always more prominent than in any other form of anæmia of a like severity. This shows that nucleated corpuscles are not to be thought of as evidence (like deformities in shape) of regenerative or degenerative conditions only. A special connection to the wide circulatory channels of leukæmic marrow seems indicated, all the more so as in the lymphatic form of the disease in which the bone marrow is usually much less affected, nucleated corpuscles are much less numerous, appearing in relatively small numbers in the very acute anæmic cases and not at all in those which are not anæmic. The protoplasm of the erythroblasts is usually polychromatophilic, contrasting in this respect with the acidophilic protoplasm of embryonic and infantile erythroblasts.

The variations in size and shape correspond to the degree of anæmia present; occasionally, *i.e.*, in cases seen early in the course of the disease, the red cells are quite normal.

As the count of the white cells rises, that of the red may fall, and *vice versa;* or the red cells may remain at a comparatively high figure despite the progress of the white.

WHITE CELLS.

Quantitative Changes.

The average number per cubic millimetre in the forty-nine cases of Table VII. (the lymphatic cases being excluded) was 385,808 at the time when the cases first came under observation. The highest count in this series is 1,072,222 and the lowest 98,000.

Among the older recorded cases are some in which the white cells were said to be more numerous than the red. The average ratio in my series is about one white to seven red. The highest ratio is 1: 2, and the lowest 1: 37. It is best to use the "red coun-

TABLE VIII.—MYELOID LEUKÆMIA.

No.	Red cells.	White cells.	PERCENTAGE.								Normoblasts seen while counting them.	Megaloblasts seen while counting them.	Date.
			Hæmoglobin.	Polymorphonuclear neutrophiles.	Small lymphocytes.	Large lymphocytes.	Eosinophiles.	Myelocytes.	"Mastcellen."	Transitional neutrophiles.			
1	2,010,000	716,000	30	40.0	1.0	10.0	4.0	42.0	3.8	Many	Many	Many	Nov. 1st, 1897.[1]
	1,720,000	732,000	..	....	....	....	....	....	......	......	......	......	Nov. 3d, 1897.
		708,000	..	....	....	....	....	....	......	......	......	......	Nov. 12th, 1897.
2	4,125,000	253,900	55	....	....	....	....	....	......	......	......	......	July 16th, 1895.
		200,000	..	....	....	....	....	....	......	......	......	......	July 25th, 1895.
	4,016,000	646,000	..	56.5	7	4.5	4	28	Many	Many	3	1	Jan. 21st, 1897.
	4,592,000	448,000	60	46	1.5	14.5	1.5	33.5	"	"	2	0	Feb. 8th, 1897.
				46.6	1.4	10.4	2.2	36.7	"	"	3	0	Feb. 17th, 1897.
3	2,960,000	175,800	42	17	3	11	19	49	"	"	13	31	July 15th, 1897.
	3,184,000	264,000	38	....	....	....	....	....	......	......	......	......	July 29th, 1897.
	3,156,000	276,000	40	....	....	....	....	....	......	......	......	......	Aug. 5th, 1897.
4	3,400,000	111,000	35	27.2	10.5	26	3	25	Many	Many			
5	3,670,000	183,090	..	31	15	8	5	32	"	"			
6	3,100,000	430,000	48	....	....	....	....	....	......	......	......	......	Aug. 10th, 1896.
	3,080,000	405,000	40	72.2	2	3.6	2	17.4	Many	Many	5	9	Aug. 31st, 1896.
7	2,520,000	510,000	50	51	.6	2	4	42.4	"	"	......	......	Jan. 22d, 1896.
		528,000	..	....	....	....	....	....	......	......	......	......	Jan. 22d, 1896.[2]
		570,000	..	....	....	....	....	....	......	......	......	......	Jan. 23d, 1896.
		560,000	..	....	....	....	....	....	......	......	......	......	Jan. 24th, 1896.
8	4,016,000	800,000	58	55	5	4	4	34	Many	Many	......	......	June 4th, 1894.
		26,000	..	....	....	....	....	....	......	......	......	......	Aug. 10th, 1894.
9	2,792,000	139,600	..	50.4	18.9	.2	6.1	24.4	......	......	......	......	April, 1893. Later the count of leucocytes was normal for several months.
10	2,715,000	394,000	..	44	1.5	1	2.5	51					
11	2,256,000	340,000	..	62.3	3.8	1.8	1.8	30.3					
12	4,288,000	213,000	37	53.8	2.2	2.8	14.4	18	8.8				
13	2,921,600	492,800	..	61	3	0	3	33					
14	3,010,000	188,000	..	37	23	6	8	26					
15	2,996,000	134,400	..	46	1.5	0.5	4	48					
16	4,800,000	220,500	..	62	1.5	1	2.5	33	......	......	......	......	Jan. 22d, 1896.
	3,060,000	274,000	41	33	10	11.5	3	42.5	......	......	......	......	June, 1897.
17	2,016,000	260,000	..	26	8	1	5	60					
18	2,576,000	748,000	..	46	2	0.5	1.5	50					
19	2,448,000	168,800	42	45	3	3	3	46					
	2,120,000	190,000											
		188,600											
	2,528,000	159,000	45										
20	5,120,000	134,000	78	74.2	4	4	2.8	15	......	......	4	1	Feb. 22d, 1896.
	5,000,000	137,800	..	....	....	....	....	....	......	......	......	......	Feb. 25th, 1896.
	4,800,000	138,000	..	61	6	2.2	2.5	28	......	......	......	......	Feb. 28th, 1896.
21	4,140,000	141,000	53	58	3	....	3.1	35	0	......	4	2	
	2,825,000	410,000	35	48	17	2	3	28	2	......	4	1	
	2,175,000	441,000	36	43	2	18	7	28	2	......	6	5	
22	2,952,000	324,000	40	33	5	5	7	21	14	15	......	......	5.4 per cent. of the lymphocytes have the characteristics of Türck's "Reizungsformen."
23	3,090,000	186,000	38	57	1.2	3.2	4.2	28	5.2	......	8	2	
24	3,020,000	454,000	45	47	2	2.6	.2	48	2	......	1	0	
25	3,170,000	260,000	35	41	3.8	1.2	8.8	43	2.4	......	4	0	Oct. 4th, 1899.
		317,000	40	53	1.8	1.4	8.2	33	2.6				
26	2,706,000	290,000	31	27	3	13	1.8	40	15	......	1	2	Oct. 21st.
		260,000	31	24	3.8	12	1.2	45	14	......	2	3	Nov. 3d.
	2,002,000	278,000	35	33	4.4	12	.4	40	11	......	4	4	Nov. 19th.
	2,631,000	289,000	31										

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[1] Many cells on border-line between large lymphocytes and myelocytes and between these and polymorphonuclear neutrophiles.

[2] Cerebral hemorrhage. Death January 25th, 1896.

TABLE VIII.—MYELOID LEUKÆMIA (*Continued*).

No.	Red cells.	White cells.	Percentage.								Normoblasts seen while counting them.	Megaloblasts seen while counting them.	Date.
			Haemoglobin.	Polymorphonuclear neutrophiles.	Small lymphocytes.	Large lymphocytes.	Eosinophiles.	Myelocytes.	“Mastzellen.”	Transitional neutrophiles.			
27	1,756,000	347,900	23	35	3	5	2	54	0	......	2	3	First day.
		418,000	..	41	2	6	2	48	0	......	11	4	Phthisis also fourth day.
28	2,500,000	248,000	..	27	2	0	9	23	4.5	25	4	2	Türck's "Reizungsformen" 9.5 per cent.
29	....	......	..	32	4	4	5	55					
30	....	......	..	49.6	3.6	2.2	6	38.6					
31	....	......	..	30	10	5	5	45	10				
32	....	......	..	54	8	0	5	34					
33	....	......	..	47.5	24.5	5	1.5	27.5					
34	....	......	..	36	4	4	28	28					
35	....	......	..	57.5	0	1.5	3.7	36	1.5				
36	....	......	..	42	5	3	1	47	2				
37	3,832,000	274,000	55	53.2	9.6	1.8	....	27.6	3.2	4.6	3	......	April 8th.
	....	282,000	..	....	....	....	....	....	......	......	......	......	April 10th.
	....	301,000	..	....	....	....	....	....	......	......	......	......	April 12th.
	....	356,000	..	....	....	....	....	....	......	......	......	......	April 14th.
38	3,572,000	236,000	60	68.6	3.1	2.1	1.3	24.9	......	......	6	......	April 2d.
	....	242,000	..	....	....	....	....	....	......	......	......	......	April 4th.
	2,728,000	258,000	55	67.9	3	4.1	2.6	22.6	......	......	8	......	April 11th.
	3,228,000	186,000	45	68.8	2.1	4.8	2.4	21.9	......	......	8	......	April 22d.
	....	220,000	45	....	....	....	....	....	......	......	......	......	April 26th.
	3,128,000	380,000	45	65.6	3.1	5.2	1.1	25	......	......	6	......	April 28th.
	3,658,000	260,000	55	61.5	12.1	8.2	2.1	16.1	......	......	2	......	May 5th.
39	3,584,000	160,480	35	52	2	4.4	1.6	40	......	......	15	3	Nov. 5th.
	3,096,000	174,000	..	49	7*	....	17	....	......	......	8	......	Nov. 9th.
40	3,232,000	420,000	50	58.9	0.9	4.2	1.1	33.1	1.4	......	3	0	March 30th.
	3,220,000	320,000	65	63.2	5	1.7	2.1	29.5	......	......	3	2	April 7th.
41	2,628,000	448,000	40	49	1.5	14.5	1.5	33.5	......	......	30	10	April 22d.
	....	418,200	40	52.4	3.9	10.8	2.1	30.8	......	......	10	8	April 26th.
	2,228,000	464,000	35	44.2	10.2	15.1	1.9	28.6	......	......	12	2	April 28th.
													May 4th.
Av.	3,123,000	325,000	43	47.5	5.2	5.4	4.4	32.5	5				

* Large and small lymphocytes counted together.

ter" with a dilution of 1: 200 in counting the white cells, otherwise they are often too crowded for convenience. Hayek [1] and Da Costa [2] have shown that the leucocytes may vary enormously in a few hours; *e.g.*, 10 A.M., 122,500; 4 P.M., 235,000; or again, 10 A.M., 730,000; 4 P.M., 547,500.

In the fresh specimen we notice that a large proportion of the white cells are but slightly amœboid, a point of marked contrast with leucocytosis, in which the leucocytes are actively amœboid. This is due to the fact that the myelocytes which form so large a

[1] Hayek: Wien. klin. Woch., 1897, No. 20.

[2] Da Costa: *Loc. cit.*, p. 251.

portion of the leucocytes in this disease possess little power of amœboid motion.

With or without the influence of therapeutic agencies or after splenectomy the white cells may fall gradually to normal and remain there for some time. The patient's symptoms may simultaneously ameliorate, or there may be no improvement but rather the reverse. Such a case occurred under my observation, and the patient, a washerwoman, went back to work and afterward passed through an attack of lobar pneumonia in safety.

At such a time, when no increase in the white cells is present, we should never suspect leukæmia, seeing the case for the first time, unless we chance to make a differential count; then the characteristic qualitative changes (see below) may be found, or the blood may be wholly non-leukæmic, as in a case recently reported by McCrae, and in a similar case slides from which were recently shown me by Martin.

Qualitative Changes.

1. *Myelocytes.*

The enormous number of myelocytes is the chief point of interest. The average in my 41 cases was 32.5 per cent (see Table VIII), rising in one case as high as 60 per cent and only 4 times falling lower than 20 per cent, but they may fall as low as 7.1 per cent (31,950 absolutely), as in one of Da Costa's cases.

Taking the average total number of leucocytes as 325,000 per cubic millimetre, the absolute number of myelocytes averages over 123,000 per cubic millimetre. So far as I am aware, the highest count of myelocytes in any other disease is that mentioned on page 438 in a case of malignant disease, namely, 4,514 per cubic millimetre.[1] The contrast is sufficiently striking. I wish to insist upon this point, namely, that the blood of myeloid leukæmia is absolutely peculiar and characteristic, and could not possibly be confused with that of any other disease. Certain writers of late years have concluded that because myelocytes do occur in a great variety of diseases other than leukæmia, therefore there is nothing peculiar about the blood of the latter affection. It would be as logical to say that because albumin and casts occur occasionally in the urine of persons practically well, therefore there is nothing characteristic about the urine of acute nephritis.

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[1] Taylor reports a gastric cancer with 4,285 per cubic millimetre.

At the first glance the stained specimen of leukæmic blood seems to be composed mostly of myelocytes, but this is because they are on the average so much larger than the other forms of white cells, which, being packed away in the interstices between the large myelocytes, do not appear prominently at first sight.

Although (as just mentioned) the average size of the myelocytes is greater than that of any other kind of leucocyte, there is a great range of variation in their size, and some are hardly, if at all, larger than a red cell. (This is equally true of the myelocytes as seen in the bone marrow. See page 65.)

The individual characteristics and variations in the myelocytes have been already sufficiently described on page 64.

2. *Polymorphonuclear Cells.*

Absolutely the number of these cells is greatly increased, although the number in each 1,000 leucocytes is considerably diminished. The actual number per cubic millimetre averages over 200,000 in my series, and in all but one of Taylor's 17 there were 65,000 or more. The average percentage in the 41 cases of Table VIII. is 47, the figures ranging between 17 and 72 per cent.

The individual cells show a much greater range of variation in size, staining properties, and the size and shape of the nucleus than in any other condition. In most forms of leucocytosis, for example, one polynuclear cell looks very much like another, but in this form of leukæmia we are often struck by—

(*a*) *Very small* cells or *very large* cells (4 μ to 20 μ in diameter).

(*b*) *Dark-stained* or very *pale-stained* cells.

(*c*) Unusual shapes in the nuclei.

(*d*) Variations in the size and staining of the granules. While normal polynuclear cells have granules nearly of one shade, the leukæmic polynuclear cells have granules varying from yellow or pink to purple or blue. Their size also varies greatly. Taylor found some as large as eosinophilic granules.

Besides these variations, we often see cells apparently belonging to this type, but whose protoplasm shows no color or granulation whatever. Other cells show a few granules scattered about against a perfectly white background. Such cells may contain basophile granules besides the neutrophile.

(*e*) There are always some cells on the border-line between the polymorphonuclear and the myelocyte, and in regard to which decision must be arbitrary. I have lately been in the habit of classifying such cells as *Transitional Neutrophiles.* Similar cells are found in leucocytotic and anæmic blood (see page 102.)

3. Lymphocytes.

In percentages the lymphocytes are reduced from their normal, 20 to 30 per cent, to an average of 10.6 per cent, as in leucocytosis. But still if we class together large and small forms, their absolute number is always increased. Thus the lowest percentage present in Table VIII. (namely, two per cent) would mean 6,500 out of the average 325,000, the total leucocyte count per cubic millimetre, and this is three or four times as many lymphocytes per cubic millimetre as are present in normal blood.

The proportion of large and small forms varies a great deal. Da Costa found an average of 12 per cent large and 4.5 per cent small in his 12 cases. Sometimes the lymphocytes in this form of leukæmia do not differ from those of normal blood, but in most cases we find the following atypical varieties:

(*a*) Large lymphocytes with a protoplasm so darkly stained that it is difficult to distinguish them from myelocytes. Indeed in some cases, when hints of a granular look appear in the violet-stained rim, we find it impossible to be sure whether we are dealing with a large lymphocyte or a myelocyte. The personal equation alone decides. These cells are not peculiar to leukæmia. Türck has described them (under the name of "*Reizungsformen*") in most infectious diseases, and I have often seen them in the blood of malignant disease and of pernicious anæmia. Taylor and Weil class them as myelocytes without granules.

(*b*) Cells like lymphocytes except that they contain a varying number of granules of one or more varieties (basophilic, acidophilic, or neutrophilic).

4. Eosinophiles.

Like all the other varieties these are *absolutely* much increased. Relatively—by percentages—they may or may not be so. In my series they ranged from 1 to 19 per cent, averaging 4.4 per cent, a slight increase over the normal.

Many writers, wrongly interpreting Ehrlich's observations on this point, have stated that an increased *percentage* of eosinophilic cells was the distinguishing mark of leukæmia, and even recent writers (*e.g.*, Gilbert, Strümpell) continue to repeat this false statement.

The cell most characteristic of splenic-myelogenous leukæmia is not the eosinophile but the myelocyte. Nevertheless eosinophiles are enormously increased absolutely, and this fact may be of great diagnostic value. In a case of cancer of the marrow with anæmia and leucocytosis Epstein[1] found large numbers of myelocytes and nucleated red cells, but no eosinophiles. The absence of eosinophiles in this case sufficed to exclude leukæmia.[2]

We distinguish several types of eosinophiles in leukæmic blood.

(*a*) Ordinary (polymorphonuclear) eosinophiles.

(*b*) Eosinophilic dwarf cells and giant eosinophiles. In some of these the granules are also huge—even 2 μ in diameter (Taylor).

(*c*) Eosinophilic myelocytes.

(*a*) Needs no comment; (*b*) is simply a very small cell with eosinophilic granules; sometimes such cells are not over 5 μ in diameter. They are not uncommon in this form of leukæmia and are very rare in any other disease. The same is true of (*c*), the eosinophilic myelocytes which are very rare in any other disease, except pernicious anæmia, in which they are occasionally seen.

These cells are like myelocytes except that their granules are eosinophilic instead of neutrophilic (see Plates I. and II.). They are found in the marrow in considerable numbers and may constitute the majority of the eosinophilic cells in this form of leukæmia. Occasionally we see eosinophiles with a few basophilic or neutrophilic granules as well. Eosinophilic myelocytes are of constant occurrence and great diagnostic value in leukæmia. In no other disease are they equally numerous. Their size, like that of the neutrophilic myelocytes, varies from 8 to 25 μ diameter.

5. *Basophiles.*

(*a*) The lymphocytes may contain basophilic granules as in any ordinary blood.

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[1] Epstein: Zeit. f. klin. Med., 1896, vol. xxx.

[2] Yet Hirschfelt and Alexander (Berl. klin. Woch., 1902, No. 11) report a case of myelogenous leukæmia (with autopsy) in which both eosinophiles and mast cells were absent from the circulating blood.

PLATE II.

FIG. 1.—Both this and Fig. 2 are intended to be fac-similes of actual microscopic fields.

(*a*) Note the cell between those labelled 8 and 9—apparently a "mast cell." Such cells are often seen in this form of leukæmia. With Ehrlich's stain they present this appearance. Basic stains bring out coarse blue granules in the periphery of the protoplasm.

(*b*) Note also the cell at the extreme upper right-hand corner of Fig. 1, which it is almost impossible to classify either as a myelocyte or as a polymorphonuclear neutrophile, since it *appears* to be intermediate between the two varieties.

(*c*) Both the nucleated corpuscles are normoblasts; 9 has polychromatophilic protoplasm. The red cells show scarcely any deformities and very slight deficiency in coloring matter.

FIG. 2.—(*a*) Note the deformities in size and shape of red corpuscles, owing to the anæmia present.

(*b*) No lymphocytes are figured, as they made up only two per cent of the white cells in this case. Eosinophiles were absent.

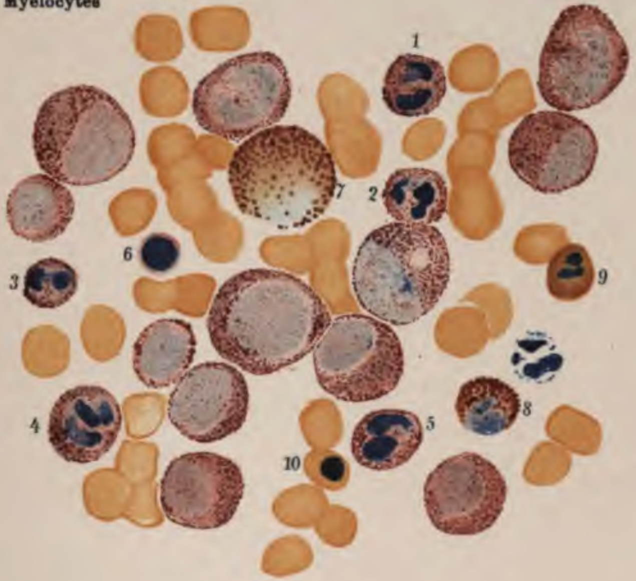
(*c*) Note that the contrast between this figure (leucocytosis) and the one above it (leukæmia) is not in the abundance of white cells but in the *kind* of white cell predominating among those present.

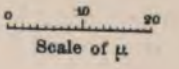
Examination of the Blood.

PLATE II.

Figure I = Splenic-myelogenous Leucaemia
Figure II = Leucocytosis (cancer of kidney)
Cells stained yellow = Red corpuscles
1. 2. 3. 4 a. 5 = Polymorphonuclear neutrophiles
6 = Lymphocyte
7 a. 8. = Eosinophiles
9 a. 10 = Nucleated red corpuscles
All others = Myelocytes

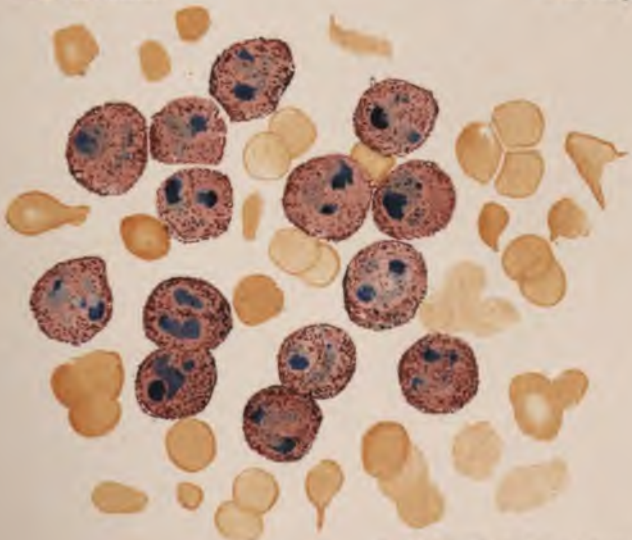
Figure I
Leucaemia.





Cells stained yellow = Red corpuscles
All others =
Polymorphonuclear-neutrophiles

Figure II
Leucocytosis.



R. C. Cabot fec.

Lith. Anst. v. E. A. Funke, Leipzig.

(*b*) The basophilic or amphoteric tendency of the granules of some of the myelocytes has been already described (page 64).

(*c*) "*Mastcellen,*" or coarsely granular basophiles, usually with a trilobed nucleus, are almost always to be found in specimens stained with Wright's stain. With the triple stain their protoplasm is nearly unstained, but usually a number of round *white* spots can be made out against a faintly stained background. These are the basophilic granulations. Mast cells make up from one to ten per cent of the leucocytes in most cases of myelocytæmia. Ehrlich states that they are always present and greatly increased in such cases, but my experience and that of Taylor do not confirm this. In 2 of Taylor's 11 cases mast cells were absent. On the other hand, one of his cases showed over 140,000 mast cells per cubic millimetre (10 per cent), and it is undoubtedly true that "an excess of mast cells is one of the most trustworthy signs of myelogenous leukæmia." Their granules are not purely basophilic but metachromic.

6. *Mitoses.*

Leucocytes showing mitosis are very rarely found in leukæmic blood and play a negligible part in the increase of the circulating leucocytes. They have no value in diagnosis.

7. *Polymorphous Condition of the Blood.*

Weiss has rightly insisted on the fact that in this type of leukæmia the blood preparations show a very *polymorphous* condition. There are no fixed types, but every variety shades through intermediate forms into some other variety. No two cells are alike. Precisely the same conditions obtain in the normal marrow, and we can scarcely resist the impression that in this form of leukæmia we see in the blood unfinished cells of various kinds which usually do not appear in the circulating blood.

As Charcot-Leyden crystals have no diagnostic value and are not peculiar to any disease, no description of them will be given here. They appear to be present wherever eosinophiles are plentiful, *e.g.*, in asthma, gonorrhœa, in the bone marrow, etc.

8. Remissions.

During remissions, when the leucocyte count may fall to normal, the percentage of myelocytes usually remains large and the diagnosis could thus be made even if we saw the case then for the first time. This I have observed in two cases, and Thayer and Taylor have had the same experience. But occasionally myelocytes and all other evidence of leukæmia disappear, and diagnosis in such remissions is impossible. McCrae and Martin have studied such cases. During such "remission" occurring in anæmic cases the blood may take on almost or quite all of the features of pernicious anæmia. Two such cases have recently been reported by Stengel (*Med. News*, October 20th, 1902).

9. Atypical Forms.

Schwartz (*Zeit. f. Heilk.*, November, 1901) has studied a case which at the first examination showed 40,000 leucocytes, 87 per cent of which were polynuclear, with 7 per cent lymphocytes and 6 per cent eosinophiles. Erythroblasts were numerous. Later myelocytes appeared and the erythroblasts disappeared.

II. LYMPHÆMIA.

(*Lymphatic Leukæmia.*)

The cases may be acute or chronic.

The writer has watched seven cases of typical lymphatic leukæmia for periods of from seven months to three years. One patient came over thirty miles from time to time to report. His blood showed little variation from the following figures: Red cells, 2,300,886; white cells, 112,000. The differential count always showed the overwhelming majority (over ninety per cent) of small lymphocytes characteristic of the disease. The lymph glands were all much enlarged, the spleen just palpable. The patient kept about his work as gardener for over two years. Another, in an active wine merchant, was wholly unattended with symptoms. The patient first sought advice for the unsightly glands in his neck. He continued to feel absolutely well and to work hard until life was

PLATE B.

Fig. 1.—Shows Normal Red Cells and Sixteen Polynuclear Leucocytes, the latter drawn somewhat too large in comparison with the red cells.

Fig. 2.—From a Chronic Case. In some acute cases the lymphocytes are larger.

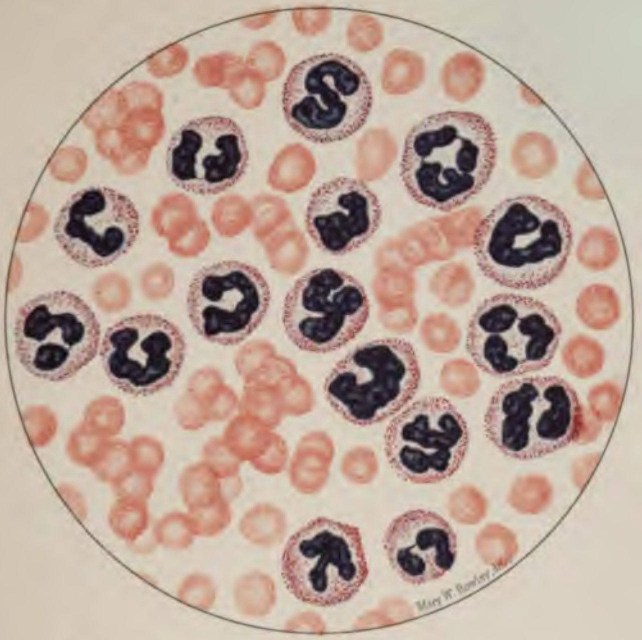


Fig. 1. LEUCOCYTOSIS, (50000 per cu. m.m.)
(Wright's modification of Leishman's stain.)

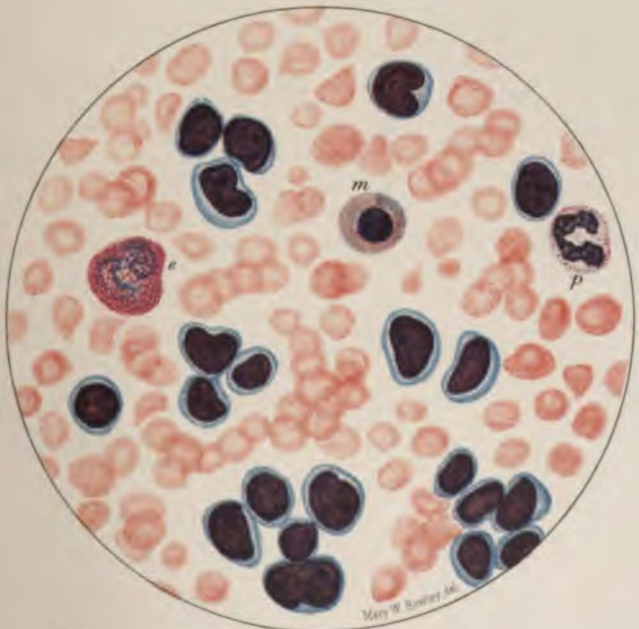


Fig. 2. LYMPHAEMIA, (LYMPHATIC LEUCAEMIA)
m. – megaloblast. e – eosinophile p – polynuclear
The rest of the white cells are lymphocytes
(Wright's modification of Leishman's stain.)

Geo.H.Walker & Co. Lit

suddenly cut short by an attack of pneumonia. I watched his blood for three years, and it always showed typical lymphæmia without anæmia. Grawitz has watched a similar case for over four years.

The blood of acute lymphæmia differs as a rule in many cases from that of the chronic types. These differences will be referred to later on.

RED CELLS.

The count of red cells is often somewhat lower than in the splenic-myelogenous form of the disease, averaging 3,600,000 in my cases. In acute cases it is usually very low and the anæmia progresses rapidly. In the infantile cases collected by McCrae, the highest count was 2,350,000. In chronic cases the red cells behave about as in myelocythæmia, except as regards nucleated forms.

A point of interest *in chronic cases* is the *rarity of nucleated red cells*, the abundance of which is so marked a feature of splenic-myelogenous leukæmia. They may follow the grade of anæmia present. In other cases (as in one reported by McCrae) nucleated red cells are entirely absent, despite a reduction of the red cells to 1,680,000. In the eleven cases in infants collected by McCrae, there were no nucleated red cells found in seven. In *acute cases* the number of nucleated forms is often greater and may be as great as in myeloid leukæmia. Two cases recently reported by Herrick[1] exemplify this.

WHITE CELLS.

Quantitative Changes.

As a rule the numerical increase is not so marked as in the splenic-myelogenous form. The average ratio of white to red cells is about 1:50 instead of 1:7, and we rarely see counts reach the height common in the other form of the disease. The highest count of my series was 1,480,000 at the patient's first visit, and the lowest 30,000, the average being 350,000 as compared with 438,000 in the myeloid leukæmia. These figures refer to uncomplicated cases.

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[1] Journal of the American Medical Association, July 24th, 1897.

Qualitative Changes.

1. *Lymphocytes* (small forms, large forms, or a mixture) make up usually over ninety per cent of all the leucocytes present. In some cases they are all nearly of one size, while in others we find every gradation from the smallest to the largest, so that it is absolutely futile to attempt to separate them into "large" and "small." Four of my cases were made up wholly of the small forms, all under 10 μ in diameter, two were composed largely of forms over 15 μ in diameter, while six showed every intermediate size.

TABLE IX.—LYMPHATIC LEUKÆMIA.

No.	Red cells.	White cells.	Per cent. hæmoglobin.	Small lymphocytes.	Large lymphocytes.	Polynuclear neutrophiles.	Eosinophiles.	Myelocytes.	Normoblasts.	Megaloblasts.	Remarks.
1.....	4,877,000	132,000	....	75.8	16.	4.6	1.6	2.	4	1	Subacute; ten weeks.
2.....	912,000	23,000	17	15.	82.	2.4	.1	.5	.....	..	Jan. 24th, 1896.
	1,440,000	43,600	23	.....	....	.....	....	....	.....	..	Jan. 26th, 1896. Acute two weeks.
	1,336,000	92,000	20	25.4	73.2	.5	.1	.8	3	1	Jan. 27th.
	1,100,000	120,000	....	.....	....	.....	....	....	.....	..	Jan. 28th. Death; autopsy.
3.....	3,000,000	31,600	....	68.5	28.	3.2	.2	....	.....	..	April 3d, 1896.
	3,500,000	31,500	55	78.	15.6	5.6	.2	.6	.....	..	April 5th, 1896.
	3,608,000	28,500	55	95.3	*	4.3	.3	....	.....	..	April 6th, 1896.
		40,000	....	.....	....	.....	....	....	.....	..	April 7th, 1896. Acute; five weeks.
		31,500	....	95.5	*	4.	.5	....	2	2	April 8th, 1896.
	4,700,000	40,000	....	.....	....	.....	....	....	.....	..	April 12th, 1896.
	3,100,000	3,400	....	39.	52.	9.	....	....	.....	..	April 22d (sepsis — semicomatose).
		800	....	94.7	*	5.3	....	....	.....	..	April 23th. Death.
4.....	2,960,000	1,480,000	....	87.9	12.	.1	....	....	.....	6	March 21st, 1897. Chronic.
5.....	4,160,000	80,000	....	80.5	2.1	17.2	....	.2	.....	..	Oct. 26th, 1896. Chronic.
	2,768,000	77,500	50	88.7	1.6	9.4	.2	.1	.....	..	Nov. 5th, 1896.
		51,800	....	.....	....	.....	....	....	.....	..	Nov. 7th, 1896.
				90.4	1.4	8.	.2	....	.....	..	Nov. 15th, 1896.
		79,500	....	.....	....	.....	....	....	.....	..	Nov. 17th. Died December, 1897.
6.....	3,520,000	64,000	60	94.	....	6	....	....	.....	..	Chronic.
7.....	2,653,000	164,000	45	2.	92.3	3.2	0	2.5	0	1	Positive Widal reaction, typhoid? — 1,000 leucocytes counted.
	2,477,500	167 500	40	.....	....	.....	....	....	.....	..	Second day.
		90,200	....	.....	....	.....	....	....	.....	..	Third day. Death.
8.....	4,078,000	738,000	41	98.6	*	.8	.6	0	0	0	July 21st; 500 cells counted.
	....	708,000	....	.....	....	.....	....	....	.....	..	July 23d.
	....	722,000	....	99.2	*	.8	0	0	0	0	Aug. 5th; 500 cells counted.
	4,196,000	760,000	39	98.1	1.2	.5	.1	.1	0	0	Oct.; 1,000 cells counted.
9.....	2,612,000	176,000	40	61.4	34.	4.6	0	0	1	0	Oct. 23d; 500 cells counted.
	3,283,000	393,000	40	50.	47.	2.8	.2	0	0	0	Nov. 16th; 500 cells counted.
10.....	5,837,000	124,000	95%	94.	0	6	0	0	0	0	Nov. 24th, 1898.
11.....	5,630,000	180,000	95	98.	0	1.9	.1	0	0	0	May 26th, 1900.
	....	500,000	....	97.	0	3	0	0	0	0	Sept. 28th, 1900.
	....	800,000	55	99.	0	.8	.2	0	0	0	Nov. 23d, 1900.
12.....	2,500,000	800,000	40	99.99	0	.0001	0	0	0	0	One polynuclear in 8,000! All the rest = lymphocytes.
13.....	5,178,000	20,000-60,000	95	80-90	5-8	10-15	0	0	0	0	Examined once a month for three years; excellent health throughout; died of pneumonia, Feb., 1901.

TABLE IX.—LYMPHATIC LEUKÆMIA (*Continued*).

No.	Red cells.	White cells.	Per cent hæmoglobin.	Small lymphocytes.	Large lymphocytes.	Polynuclear neutrophiles.	Eosinophiles.	Myelocytes.	Normoblasts.	Megaloblasts.	Remarks.
14.....	....	....	....	94.0	*	5.7	....	0.37	......	..	Chronic.
15.....	....	....	....	97.9	7.	1.4	.8	....	2	..	Acute.
16.....	....	....	....	86.2	7.	9.8	....	....	......	..	History unknown.
17.....	....	....	....	72.	......	28.	....	....	......	..	History unknown.
18.....	....	....	....	99.6	*	.4	....	....	Few.	..	History unknown.
19.....	....	....	....	92.2	*	7.8	....	....	......	..	History unknown.
20.....	700,000	600,000	10	99.8	*	.2	....	....	3	..	2,500 cells counted.
21.....	3,870,000	730,000	25	86.5	5.5	7.5	....	....	2	..	July 21.
	3,400,000	131,600	40	87.25	4.25	8.25	.25	....	4	..	July 27.
	2,384,000	111,000	40	81.5	1.5	16.5	.5	....	......	..	Aug. 6.
	2,550,000	168,000	55	76.75	4.5	18.	.25	....	2	..	Aug. 12.
22.....	3,656,000	154,000	50	87.64	3.7	7.5	1.2	....	2	4	Sept. 29.
		129,000	50	......	......	......	....	....	......	..	Sept. 29.
	3,524,000	124,000	54	54.	25.2	16.4	.6	....	1	6	Oct. 1.
		91,000	....	......	......	......	....	....	......	..	Oct. 3.
		87,000	....	......	......	......	....	....	......	..	Oct. 6.
Av'age	3,170,000	240,000+	40	80.2	15.	4.2	.2	.4			

* Large and small forms counted together on account of the impossibility of differentiating them in these cases.

In acute cases, in which the large cells usually predominate, the staining is often very faint throughout the nucleus and protoplasm (see Plate III., *b*), so that at first sight we should think something was wrong with our technique. Other leucocytes in the same preparation, however, will stain normally, showing that the trouble is in the lymphocytes and not in the technique. These large lymphocytes are identical in their appearance with those found at the "germ centres" of all adenoid tissue, and probably are the mother cells of the small lymphocytes. Benda has termed them "lymphogonien." They have often been mistaken for myelocytes, from which they are to be distinguished by the absence of any neutrophile granulation. They often show evidences of degeneration (see page 66). The protoplasm may be entirely unstained as in most of the cells in Plate III., *b*, or it may stain pale gray or pink. In other specimens, especially those of the small-cell type (Plate III., *a*), the lymphocytes stain well. Their nuclei are frequently indented or even divided in two (this occurs also in normal blood, but less often).

Fraenkel believes that if a chronic case takes on acute symptoms the blood becomes more lymphæmic, while if a case starts acute and becomes chronic the lymphocytes decrease. Thus a case reported by v. der Wey[1] of chronic myeloid leukæmia six weeks before death began to have fever, hemorrhages, great increase in the total leucocyte count and in the anæmia. No complication was present. The lymphocytes increased 30 per cent, and the polymorphonuclear neutrophiles dropped from 30 to 3 per cent.

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[1] Deut. Arch. f. klin. Med., vol. lvii.

Gerhardt[1] watched a case which began acutely with a large percentage of *large* lymphocytes and then became chronic with a predominance of *small* lymphocytes.

In acute cases Litten[2] has noticed fatty degeneration in the leucocytes.

The following figures illustrate the influence of a septicæmia (from suppurating cervical glands) which ended the life of No. 3 in Table IX.

Date.	Number of leucocytes.	Percentage of lymphocytes.
April 3d	81,600	96.5
" 4th	81,000	
" 6th	28,505	98.6
" 8th	44,000	
" 10th	81,500	95.5
" 12th	40,000	
" 18th	Sepsis began.	
" 20th	5,661	
" 21st	4,000	
" 22d	8,400	92.
" 24th	8,222	
" 28th	800	
" 29th	471	94.7
Death on the 29th.		

Zeissl's case, also of the lymphatic form, showed the following:

Date.	White cells.	Percentage of lymphocytes.	Percentage of polynuclear cells.
September 9th	80,000	96.	4.
" 24th	118,000		
" 26th	119,000		
" 29th	122,000	97.8	2.
October 6th	140,000		
" 9th	Pneumonia began.	99.	1.
" 10th	119,000		
" 11th	98,000		
" 12th	68,500		
" 13th	43,500	88.7	11.3
" 14th	50,000		
" 15th,	9,350	85.4	14.6
" 16th (A.M.)	133,200		
" 16th (P.M.)	172,000	75.	25.

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[1] Fifteenth Cong. f. innere Med., 1897.

[2] Eleventh Cong. f. innere Med., 1893.

PLATE III.

(*a*) ***Chronic Lymphæmia*** **with Excess of *Small* Lymphocytes.**

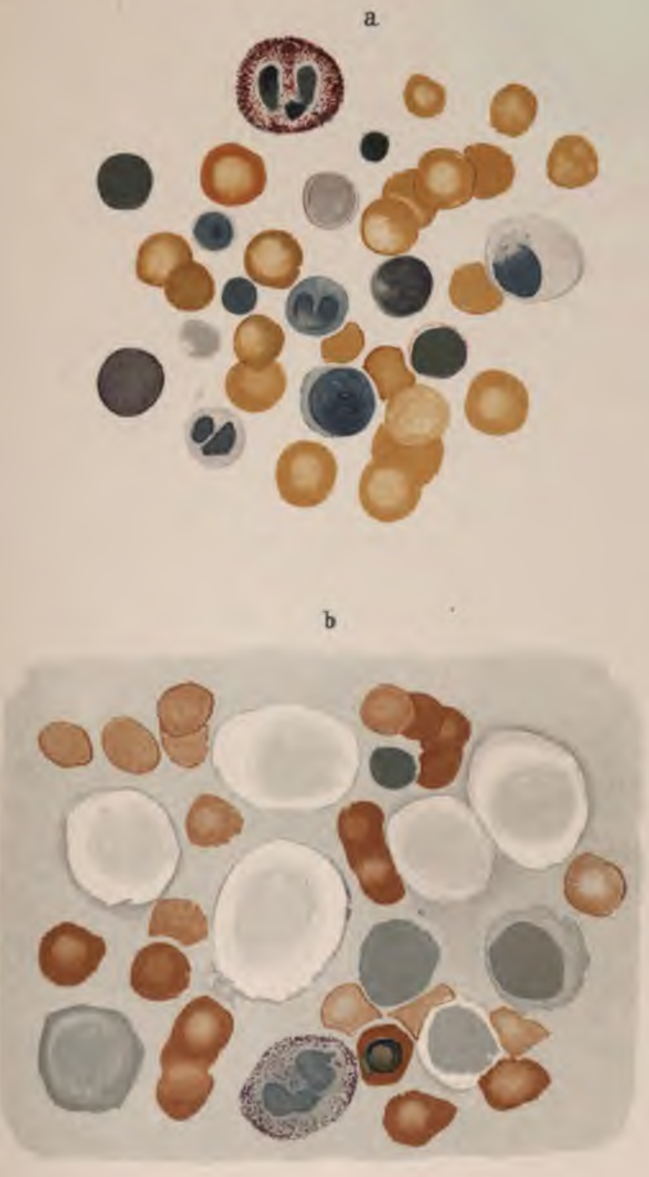
One polymorphonuclear cell is present. All the rest are lymphocytes and exemplify the variations in the morphology of the cell occurring in this and other diseases as well as in health, *e.g.*, variations in the staining of the protoplasm and nucleus, indentation and even division of the nucleus.

Note that the scale of the whole of Plate III. is larger than in the other plates (see scale of μ).

(*b*) *Acute Lymphæmia* with Excess of *Large* Lymphocytes.

Note the lack of chromatin in both nuclei and protoplasm of large lymphocytes. The plasma around them or their extreme edge took most of the stain. The brown tint of the red cells is due to underheating. Compare the colors with those in the figure above (*a*) in which the preparation was properly heated.

PLATE III.



Lymphatic Leucaemia

a. Small Lymphocytes in excess
b. Large „ „ „

0 10 20
Scale of μ

R. C. Cabot fec.

Lith. Anst. v. E. A. Funke, Leipzig.

Polymorphonuclear neutrophiles are absolutely as well as relatively diminished in most cases. Indeed they are often so scarce that one has to look through several thousand leucocytes before finding one. There is nothing abnormal about them—a point of marked contrast with the neutrophiles in myeloid leukæmia. *Eosinophiles* and *myelocytes* are equally rare.

Summary.

The leading characteristics of leukæmic blood are as follows:

(*a*) *Myeloid leukæmia.*

1. Red cells about 3,000,000; nucleated forms very numerous.
2. White cells about 450,000, of which
3. Myelocytes form about thirty per cent.
4. Every possible form of cell *intermediate* between the ordinary varieties is to be seen. ("Polymorphous blood.")

(*b*) *Chronic lymphatic leukæmia.*

1. Red cells about 3,000,000 or lower; nucleated forms rare.
2. White cells about 300,000, of which
3. Small lymphocytes usually form over ninety per cent.
4. Myelocytes and eosinophiles very scanty.

(*c*) *Acute lymphatic leukæmia.*

1. Red cells *much* diminished; nucleated forms infrequent.
2. *Large* forms of lymphocytes usually predominate; many of them often show signs of degeneration.
3. Neutrophiles and eosinophiles very scanty.

Diagnostic Value.

Leukæmia is distinguished by the blood examination from

1. Hodgkin's disease: (*a*) splenic, (*b*) glandular.
2. Tumors of the spleen and vicinity (*e.g.*, kidney or retroperitoneal glands).
3. Enlargements of the lymphatic glands from tuberculosis, syphilis, malignant disease.
4. Hydronephrosis.
5. Huge leucocytosis from any cause.
6. Chronic malaria.
7. Amyloid disease.

1. *Leukæmia and Hodgkin's disease* (lymphadenoma or pseudoleukæmia). The pathology of the two diseases is identical but for the blood count. In Hodgkin's disease the blood is normal, or

shows only a moderate anæmia or leucocytosis (polymorphonuclear cells alone increased), and the diagnosis is easily made.

2. *Tumors of the spleen* and especially of the *kidney* are very apt to be mistaken for leukæmia. Within a single year I was asked to examine the blood in three cases of "leukæmia," all of which turned out to be malignant disease of the kidney. In all of these there was a large tumor resembling the spleen in the left hypochondrium, also a very large increase of white cells. In two of them the blood was examined fresh and the great number of white cells in the slide taken as evidence confirmatory of leukæmia. The stained specimen, however, showed only marked leucocytosis with ninety per cent of polynuclear cells of the ordinary type and no myelocytes. Other large tumors of this region showed similar results. Occasionally cases of leukæmia with numerous metastases are described as "sarcomatosis," and then it is asserted that the blood of leukæmia is identical with that of sarcoma. The source of the mistake is obvious.

3. *Adenitis* with hyperplasia due to tuberculosis shows usually normal blood[1] and is thus easily distinguished from leukæmia. Leucocytosis is often present in syphilitic cases and still more marked in those due to cancer or sarcoma, but the counts rarely reach 30,000 and myelocytes are absent or very scanty.

4. One case of *hydronephrosis* in which the distention of the sac was so great that it presented as a hard, solid tumor on the right hypochondrium, was taken for leukæmia by a competent observer some years ago. The *normal* blood examination revealed the mistake, and excluded also malignant disease in all probability. The diagnosis was reached, however, only at the autopsy.

5. Huge leucocytosis in pneumonia or malignant disease may cross the old boundary line of 100,000 white cells, beyond which none but leukæmic cases were supposed to venture. The differential count sets us right instantly, showing ninety per cent or so of the increase to be made up of ordinary polymorphonuclear leucocytes.

6 and 7. The large spleen and cachectic appearance associated with chronic malaria and long-standing suppurations may be easily distinguished from leukæmia by the absence of anything more than anæmia and leucocytosis in the blood.

---

[1] Sometimes marked leucopenia.

	Red cells.	White cells.	Lymphocytes.	Polynuclear leucocytes.	Myelocytes.	Nucleated red cells.
Leukæmia (splenic-myelogenous).	About 3,000,000	450,000 ±	About 7.6 per cent.	About 50 per cent.	About 37 per cent.	Very numerous.
Leukæmia (lymphatic).	About 3,000,000	100,000 ±	About 96 per cent.	About 3 per cent.	Absent.	Rare.
Hodgkin's disease....	About normal.	7,500 ±	Normal.	Normal.	Absent.	Absent.
Tumors of or near the spleen.	Usually diminished.	20,000 to 40,000 ±	Greatly decreased.	Greatly increased.	Few if any.	Few.
Leucocytosis in general.	....	May be over 100,000	Greatly decreased.	Greatly increased.	Few if any.	Few at times.
Chronic malaria......	Much diminished.	Somewhat increased.	Usually increased.	Usually decreased.	Few if any.	Few.
Amyloid disease	Usually diminished.	Usually increased.	Usually decreased.	Usually increased.	Absent.	May be a few.
Hydronephrosis......	Normal.	Normal.	Normal or decreased.	Normal.	Absent.	Absent.

EFFECT OF INTERCURRENT INFECTIONS.

There are on record about thirty cases in which leukæmia (acute or chronic) has been complicated with some intercurrent infection, with marked effect upon the blood in all but one. This single case was an acute rheumatic arthritis reported by Richter in the discussion of Fraenkel's article in the *Deutsche medicinische Wochenschrift* for 1895 (Nos. 39, 43, and 45), p. 639. Here the blood remained unchanged.

Müller's[1] case of lymphatic leukæmia was complicated by a septicæmia, and the count of white cells *rose* from 180,000 to 400,000 per cubic millimetre, with a marked increase in the percentage of polymorphonuclear cells. Here was a genuine leucocytosis added to a leukæmia.

With the exception of these two cases, all those hitherto published have shown a marked progressive *decrease* in the total number of leucocytes without any change in the percentages of the different varieties in twelve, while eight showed, like Müller's, an increased percentage of the polymorphonuclear cells despite the decrease in the total leucocyte count.

Marischler,[2] in a case of lymphatic leukæmia with cancer of the kidneys, found:

	1. At First.	2. Later.
Red cells	3,450,000	2,400,000
White cells.....................	96,000	48,000
Hæmoglobin....................	50 per cent	30 per cent

---

[1] Müller: Deut. Archiv für klin. Med., 1892, vol. l., p. 47.

[2] Wien. klin. Woch., July 23d, 1896.

	1. At First.	2. Later.
Polymorphonuclear cells	15.6 per cent.	57.5 per cent.
Small lymphocytes	83.3 "	40.0 "
Large lymphocytes	1.8 "	1.6 "
Eosinophiles	.18 "	.16 "
Myelocytes	....	.16 "

Various infections—miliary tuberculosis, pneumonia, grippe, erysipelas, abscess kidney, septic lymph glands—alike decrease the leucocyte count or reduce it to or below normal. In one case a rise just before death was observed.

Thus in Henck's case the leucocytes fell from 400,500 to 89,000, in one of Müller's from 246,900 to 57,300, in Kovác's from 67,000 to 17,000, in Zeissl's from 140,000 to 9,350. I have already mentioned a case of lymphatic leukæmia (page 170) in which the leucocytes fell from 40,000 to under 500, this last being on the day of death. In this case the percentages of the different varieties of leucocytes remained entirely unchanged.

Herrick[1] reports a case complicated by acute streptococcus infection in which the white cells were 60,000 at the time of death. How high they may have been earlier is not known

It appears, therefore, that when an infection complicates leukæmia we may have—

1. No effect (see case of rheumatic fever as a complication, just mentioned).
2. A genuine leucocytosis on top, so to speak, of the leukæmia, with an increased percentage of polymorphonuclear cells.
3. A decrease in the leucocyte count with or without an increase of polymorphonuclear cells. This decrease is by far the most common result and may go far below normal as death approaches.

Goldschneider[2] found that by the injection of splenic extract and other substances he could bring about a similar diminution in the number of leucocytes, but that, as in the case of intercurrent infections, this diminution was not accompanied by any improvement in the patient's condition, and death followed as usual.

Abscesses occurring in leukæmic patients are filled with polynuclear leucocytes as ordinary abscesses are, and do not contain myelocytes.

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[1] *Loc. cit.*

[2] Discussion of Fraenkel's article.

HODGKIN'S DISEASE.

(*Pseudo-Leukæmia*, *Lymphoma.*)

The diagnosis of this disease is impossible without the blood count. Yet the blood is in no way peculiar, but presents in most cases all the characteristics of the normal tissue. Its value is as negative evidence, telling us in a given case that leukæmia is absent.

(I.) Transitions from Hodgkin's disease to leukæmia have taken place under the eyes of competent observers, but they are very rare. But few such cases are on record so far as I know—that of Fleischer and Penzoldt,[1] that of Mosler,[2] and one reported by Senator,[3] in which two sisters came under observation, both suffering from Hodgkin's disease. One died of it; in the other the blood changed to that of leukæmia before death.[4] Wende (*Amer. Jour. Med. Sciences*, December, 1901) reports a typical example of this transition.

Date.	Red cells.	White cells.	Hæmoglobin.	Remarks.
April 26th..	5,128,000	4,000	88	Typical "Hodgkin's disease." Polynuclears, 68 per cent. Lymphocytes, 27 "
July 10th...	1,936,000	34,000	..	Polynuclears, 3.4 " Lymphocytes, 95.5 "

Posselt (*Wien. klin. Woch.*, 1895, p. 407) has presented a similar case; on August, 1892, the leucocytes were 15,000, with 60 per cent lymphocytes; on April, 1893, the leucocytes were 330,000, with 80 per cent lymphocytes.

Doubtless many of the other cases supposed to exemplify a similar transition were really cases in which a leucocytosis arose owing to some inflammatory complication.

From the existence of these very rare cases of a transition to leukæmia, it has been supposed, especially by French observers, that Hodgkin's disease is simply an early stage of true leukæmia, and that this would always become apparent were it not that the patients die of some intercurrent disease before the signs of leukæmia have time to show themselves in the blood. One difficulty with this view is that there occur chronic cases which last from eight to ten years without any change in the blood. Another difficulty is that the transition is in fact rare, despite the relative frequency with which the disease is met with.

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[1] Deut. Arch. f. klin. Med., vol. xvii.

[2] Ziemssen's "Handbuch d. Path. und Therap.," vol. viii.

[3] Berl. klin. Woch., 1882, p. 533.

[4] Askanazy has recently observed the transition in a case in which the blood was normal for two and a half years and then leukæmic for one and a half years under observation (quoted by Pinkus in Nothnagel's "Specielle Path. und Therap.," vol. viii.).

(II.) Probably many cases diagnosed as Hodgkin's disease are in fact cases of glandular hypertrophy due to syphilis or tuberculosis, and this fact has led many to the belief that *all* cases called Hodgkin's disease are in reality only syphilitic or tuberculous adenitis.

In a considerable number of cases, however, tuberculosis has been disproven by careful inoculation experiments with the glandular tissue, and there is no reasonable doubt that *some* cases, at any rate, are not due to tuberculosis or syphilis. Probably the diagnosis can never be made with absolute certainty during life.[1]

(III.) The frequent occurrence of fever and other symptoms characteristic of an infectious disease has led some writers to class it as such. In a certain percentage of cases the disease (like leukæmia) has run an acute course, lasting not more than six weeks from the first symptoms to death. In some chronic cases the same sort of evidence of an infectious nature has been brought forward. Ulcerations occur in the mouth and intestine, through which morbid products might gain admission. Various bacteria (pyogenic and others) have been found in the blood and tissues from time to time, but numerous negative examinations for micro-organisms are also on record, and the evidence is insufficient to establish the infectious nature of the disease. None the less, there is a growing tendency among the leading writers and observers in Germany and elsewhere to believe that the disease will ultimately be shown to be tuberculous.

(IV.) Meantime most surgeons continue to regard it as a form of sarcoma and to treat it like malignant disease.

The Blood.

Whatever the nature of the disease, we find in the earlier stages of most cases normal blood, as will be seen in Table X. (cases 7 to 23 inclusive).

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[1] The recent monographs of Reed (Johns Hopkins Hospital Reports, 1902, vol. x., p. 133), Simmons (Journal of Med. Research, June, 1903), and Longcope (Bulletin No. 1 of the Ayer Clinical Laboratory, October, 1903, Philadelphia), have shown that there *is* a characteristic histological picture corresponding to Hodgkin's disease, and apparently to no other.

TABLE X.—HODGKIN'S DISEASE.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	28	F.	5,500,000	64,000	75	Polymorphonuclear cells, 95 per cent. Lymphocytes, 5 per cent.
2	....	M.	3,848,000	39,200	48	Acute. Diff.* 500. Polymorphonuclear cells, 95.2 per cent. Lymphocytes, 4.6 per cent.
3	24	F.	4,886,000	32,000	53	
4	19	F.	5,528,000	22,200	....	Diff. 200 cells. Polymorphonuclear cells, 86.5 per cent.
			5,160,000	25,400		Six weeks later. Lymphocytes, 12.0 per cent. Eosinophiles, 1.5
5	19	M.	2,480,000	20,200	33	Stained specimens normal.
6	26	....	....	14,000	60	June 6th.
			5,148,000	21,200	50	June 11th. Polynuclear, 92.8 per cent. Small lymphocytes, 3.6 per cent. Large lymphocytes, 3.0 " Eosinophiles, .2 " Myelocytes, .4 " No nucleated reds. Reds pale. Some few irregular in shape.
7	28	....	4,312,000	12,000	42	Polynuclear, 90.5 per cent. Lymphocytes, 7.5 " Eosinophiles, 2.0 "
8	59	....	....	8,500	68	
9	28	....	3,760,000	7,000	65	
10	34	....	3,380,000	6,800	40	Polynuclear, 84.6 per cent. Small lymphocytes, 10.0 " Large lymphocytes, 3.2 " Eosinophiles, 1.4 " Myelocytes, .8 " Normoblasts = 1
						November 21st. T. 102°.
				6,700	....	November 29th. } Red stain poorly. Fairly regular in size. Tendency to diminished size. Few large. Slight poikilocytosis.
			3,512,000	....	40	December 5th. }
				6,300	....	December 8th. }
			2,960,000	7,900	32	December 9th. }
			2,828,000	7,600	28	December 27th. }
11	27	....	....	6,200	....	
				7,200	....	February 19th. Count 300. Polynuclear, 89.0 per cent. Large lymphocytes, 2.0 " Small lymphocytes, 8.7 " Eosinophiles, .3 "
12	43	....	2,880,000	5,000	30	January 6th. Count 500. Polynuclear, 57.6 per cent. Small lymphocytes, 29.9 " Large lymphocytes, 12.5 " Eosinophiles, .7 " Mast cells, .3 " Reds rather pale. Slightly irregular in shape.
				3,800	....	January 13th.
			2,650,000	....	30	January 15th.
				5,200	30	January 31st. Polynuclear, 63.2 per cent. Small lymphocytes, 34.0 " Large lymphocytes, 2.8 " Eosinophiles, 0.0 " Megaloblasts = 1.0 Normoblasts = 0.0 Reds as before.

* Diff. = Differential count of.

TABLE X.—HODGKIN'S DISEASE (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
				3,000	30	February 8th. Polynuclear, 55.4 per cent. Large lymphocytes, 8.6 " Small lymphocytes, 36. " Eosinophiles, 0. " Reds as January 31st.
			3,252,000	3,400	30	February 13th. Polynuclear, 57.4 per cent. Small lymphocytes, 32.2 " Large lymphocytes, 6.4 " Eosinophiles, 4.0 "
			2,012,000	5,000	28	February 23d. Polynuclear, 70 per cent. Small lymphocytes, 26 " Large lymphocytes, 4 " Eosinophiles, 0 "
13	44	....	2,336,000	3,400	30	May 4th. Count 500 cells. Polynuclear, 82.0 per cent. Small lymphocytes, 15.6 " Large lymphocytes, 2.4 " Eosinophiles, 0.0 " No nucleated reds. Reds stain rather palely. Little variation in size. Slight irregularity in shape.
			2,140,000	4,000	35	May 28th. Polynuclear, 70 per cent. Small lymphocytes, 18 " Large lymphocytes, 12 " Eosinophiles, 0 " Reds similar to May 4th.
14	28	....	....	....	....	Polynuclear, 69 per cent. Lymphocytes, 26 " Eosinophiles, 5 "
15	37	M.	5,990,000	13,500	....	Polymorphonuclear cells, 95 per cent. Lymphocytes, 5 "
16	25	M.	5,440,000	9,500	59	Death; autopsy.
17	19	F.	5,724,000	6,800	42	Polymorphonuclear cells, 50 per cent. Lymphocytes, 40 "
18	Adult.	M.	3,652,000	5,800	....	Diff. 300. Polymorphonuclear cells, 50.0 per cent. Lymphocytes, 45.3 " Eosinophiles, 1.3 " Myelocytes, 1.7 " Big spleen, pallor, nosebleed, debility.
19	29	M.	5,210,000	5,000		
			3,840,000	5,600	....	Two months later.
			1,000,000	....	....	Three weeks "
20	58	M.	2,820,000	4,800	60	Polymorphonuclear cells, 80 per cent. Lymphocytes, 17 " Eosinophiles, 3 "
21	21	M.	4,560,000	4,000 5,800	....	
22	23	M.	4,210,000	3,332	....	Myelocytes, 1 per cent. Big liver and spleen. Eosinophiles, 4 "
23	....	M.	3,800,000	1,440	67	Diff. 500. Polymorphonuclear cells, 71.25 per cent. Lymphocytes, 28.00 " Eosinophiles, .75 " One normoblast.
24	....	....	....	No leucocytosis.	....	Diff. 200. Polymorphonuclear cells, 63.5 per cent. Lymphocytes, 36.5 " Eosinophiles, 1.0 " Many of the lymphocytes have two nuclei.

TABLE X.—HODGKIN'S DISEASE (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
25	....	....	....	No leucocytosis.	....	Diff. 300. Polymorphonuclear cells, 41.7 per cent. Lymphocytes, 48.4 " Eosinophiles, 9.3 " Myelocytes, .6 "
26	4	M.	....	No leucocytosis.	....	Diff. 500. Polymorphonuclear cells, 60.2 per cent. Lymphocytes, 36.0 " Eosinophiles, 3.6 " Myelocytes, .2 " Two normoblasts.
27	....	F.	....	....	....	Diff. 500. Polymorphonuclear cells, 92.6 per cent. Lymphocytes, 5.2 " Myelocytes, 2.2 " No eosinophiles.
28	....	....	....	No leucocytosis.	....	Diff. 313. Polymorphonuclear cells, 62.3 per cent. Lymphocytes, 37.0 " Myelocytes, .6 "
29	28	M.	5,218,000	11,800	85	Polynuclear, 51 per cent. Small lymphocytes, 35 " Large " 7 " Eosinophiles, 7 "
30	30	M.	5,280,000	6,800	55	Diff. Polymorphonuclear cells, 76.0 per cent. Lymphocytes, 22.3 " Eosinophiles, 1.4 " Myelocytes, .3 " No nucleated red cells.
31	32	M.	4,616,000	2,400	70	
32	....	....	....	2,200	....	Diff. Polymorphonuclear cells, 69 per cent. Small lymphocytes, 19 " Large " 18 " Eosinophiles, 4 " Few normoblasts.
33	41	....	3,520,000	12,600	47	Polymorphonuclear cells, 69.0 per cent. Nov. 23d. Lymphocytes, 28.0 " Eosinophiles, 3.0 " Polynuclear cells, 70.2 per cent. Nov. 28th. Lymphocytes, 29.0 " Eosinophiles, .8 "
34	36	....	....	21,300	90	
35	54	....	....	23,425	65	400 cells. Polymorphonuclear cells, 81 per cent. Lymphocytes, 18 " Eosinophiles, 1 "
36	58	....	4,272,000	4,400	75	
37	6	....	4,112,000	17,200	35	Diff. Polynuclear cells, 80.1 per cent. Lymphocytes, 18.8 " Eosinophiles, 1.1 "
38	6	....	1,296,000	4,100	22	Diff. Polynuclear cells, 5.6 per cent. Lymphocytes, 94.2 " Eosinophiles, .2 " Autopsy.
39	55	....	....	64,000 66,000 45,400	55	June 18th. " 20th. " 22d.
40	26	....	....	11,100	85	

TABLE X.—HODGKIN'S DISEASE (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
41	27	....	4,480,000	24,000	90	August 8th, Diff. count 633 cells. Polynuclear cells, 84.7 per cent. Small lymphocytes, 4.1 " Large " 9.6 " Eosinophiles, 1.6 " Myelocytes, .4 "
				32,000	..	August 29th.
				20,700	..	" 30th.
				5,700	..	September 1st.
				42,000	..	" 2d, Diff. Polynuclear cells, 92.8 per cent. Small lymphocytes, 1.8 " Large " 4.9 " Eosinophiles, .5 " Normoblast No. 1, Death.
42	56	....	....	25,600	75	August 15th. Polynuclear cells, 34.6 per cent. Small lymphocytes, 58.8 " Large " 5.4 " Eosinophiles, 1.2 "
				25,400	..	August 20th.
				23,000	..	" 23d, Diff. Polynuclear cells, 40.3 per cent. Small lymphocytes, 37.6 " Large " 17.0 " Eosinophiles, 5.1 "

As the disease progresses the hæmoglobin soon begins to fall, later the red cells do so, until, as at the end of Case 19 of the present series, the blood may reach the severest grade of anæmia. In acute cases the anæmia may develop very rapidly. The usual qualitative changes characterizing severe secondary anæmia may be present.

White Cells.

When inflammation arises in the glandular tumors and sometimes when none is found, the white cells may be greatly increased, even up to a ratio of 1: 80 red cells, as in Case 1 of the present series, and in the case reported by Vaquez and Ribierre (Soc. Méd. d. Hôp., 1900, p. 1191), on which between July 24th and August 27th the leucocytes rose from 35,000 to 51,000 with approximately 94 per cent of polynuclear cells throughout. There is, however, no more resemblance to leukæmia than in any other form of leucocytosis, the polymorphonuclear cells alone being increased. There is no reason for supposing, as Reinert[1] does, that relative diminution of the lymphocytes is owing to the diseased condition of the lymph glands, nor for believing with Pinkus (Nothnagel's "Specielle Path. und Ther.," vol. viii., 1901) that the *relative increase of lymphocytes* which some cases show is characteristic of Hodgkin's disease. Pfeiffer[1] has recently reported a case of the cutaneous form of the disease with 60 per cent of lymphocytes out of a total leucocyte count of 6,500.

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[1] "Die Zählung der Blutkörperchen," Berlin. 1891.

As in any other cachectic condition, small numbers of myelocytes may be found. They were seen in nine of our cases out of twenty-five in which a color analysis was made, the highest percentage being two per cent. Eosinophiles are usually decreased when leucocytosis is present.

Summary.

Normal blood in early stages.
Later often marked anæmia; sometimes leucocytosis

Diagnostic Value.

The only help given us by the blood is in excluding leukæmia.

Syphilis, tuberculosis, or malignant disease might cause similar changes or lack of changes in the blood.

EFFECTS OF SPLENECTOMY ON THE BLOOD.

When splenectomy is performed for abscess, hydatid, rupture of the spleen, or other local disease, it is followed, after a varying number of weeks, by a hyperplasia of the lymph glands, associated with *lymphocytosis.* How long this lymphæmia lasts is not altogether clear.

Later, after many months, a moderate eosinophilia may appear and the mast cells are increased. Ehrlich examined one case six months after operation in which a considerable lymphæmia existed, the back of the lymphocytes being large. Eosinophiles were not increased. In another case he found the lymphæmia persisting in the fifth year after operation, while the eosinophiles were between three and four per cent. In two other cases he found (six and eighteen months after the operation) no lymphocytosis.

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[1] Pfeiffer: Wien. klin. Woch., 1897.

In the following table the records of four other cases are given:

TABLE XI.

Case.	Red cells.	White cells.	Per cent haemoglobin.	Polymorpho-nuclear neutrophiles.	Small lymphocytes.	Large lymphocytes.	Eosinophiles.	Average diameter of red cells.	Remarks.
*1	4,570,000	8,000	63	..	..	..	..	....	Before operation.
	4,970,000	30,000	64	..	..	..	..	....	Three days after.
	5,180,000	65,000	77	..	..	..	..	....	Six days after.
	4,800,000	17,500	66	..	..	..	..	....	Forty-eight days after.
	4,353,000	11,700	85	..	..	..	..	....	Four months after.
	3,300,000	11,600	85	..	..	..	..	....	Five years after.
*2	3,200,000	53,000	65	..	..	..	..	....	(1893, for abscess.) Three weeks after.
	4,500,000	13,800	80	..	..	..	..	....	Four months after.
†3	1,634,000	12,000	45	61	16	20	3	8.1 μ	Operated (April 9th, 1893) for malarial hypertrophy with twisted pedicle. April 23d.
	2,460,000	20,000	87	49	18	32	1	....	May 6th.
	4,530,000	27,000	110	66	18	15	1	7.7 μ	May 13th, 1894.
	3,977,000	8,000	100	62	21	11	6	....	October 2d, 1895.
†4	4,850,000	30,000	108	83	8	8	1	...	Operated for hypertrophied, wandering spleen. Before operation.
	4,700,000	39,000	100	91	5	4	0	....	Seven days after.
	3,630,000	18,000	105	78	15	6	1	...	Two months after.
	2,750,000	20,000	63	84	5	10	1	....	Three years after.

* Czerny: Cited in Laudenbach: Arch. de Physiol., 1896, p. 724.
† Hartman and Vaquez: Soc. de Biol., February 5th, 1895.

One point which these cases clearly prove is that no one variety of leucocyte is supplied to the blood from the spleen.

SPLENIC ANÆMIA.

(*Pseudo-Leukæmia Splenica, Anæmia with Enlarged Spleen.*)

I object to the term "splenic anæmia," because it seems to suggest that the splenic enlargement is in some way the cause of the anæmia, and for this there is no sufficient evidence. But, whatever term is used, there is at least one point about the blood of cases of idiopathic anæmia occurring in adults[1] and associated with enlarged spleen which deserves notice. This is the leucopenia. In

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[1] I do not wish at this point to discuss the significance of similar cases in children. See page 519.

Osler's article (*Am. Jour. Med. Sciences*, January, 1900) the following counts are recorded:

Case.	Date.	Red cells.	White cells.	Hæmoglobin, per cent.	Polynuclears, per cent.	Lymphocytes, per cent.	Eosinophiles, per cent.	Remarks.
I.	Feb. 1879.	2,250,000	7,100	..	..	..	..	Recurring hæmatemesis and melæna. Death in an attack of melæna in 1897.
II.	1898.	3,000,000	2,800	25	84.4	12.8	2.8	Hæmatemesis for years at intervals. Splenectomy. Recovery.
III.	1898.	4,000,000	6,500	30	73	25	2	Hæmatemesis and melæna frequently.
IV.	1895.	4,816,000	5,000	55				
V.	1896.	3,600,000	3,000	66	66	31	1	
VI.	1897.	4,788,000	5,200	60	40	59	1	
VII.	1898.	4,128,000	2,800	45				
VIII.	1898. Jan.	3,328,000	2,000	40	78	21.5	.5	Occasional normoblast.
	June.	2,500,000	4,000	45				
IX.	1899.	4,208,000	4,000	45	65	31.2	3.3	
X.	1899. Oct. 12th.	1,540,000	3,300	23	74	23.8	1.5	Myelocytes, 1.5 per cent. While counting 300 leucocytes, saw Normoblasts, 32. Megaloblasts, 13.
	" 17th.	1,380,000	3,250	20	..	..	..	While counting 400 white cells, 75 nucleated reds were seen, 21 of which were normoblasts, 19 megaloblasts, and 35 intermediate.
	Nov. 10th.	3,120,000	4,500	55				
	" 20th.	3,680,000	4,300	54				No nucleated reds.
XI.	1899. Oct. 31st.	3,856,000	4,500	55	73.7	25.3	1	
	Nov. 16th.	3,992,000	3,500	60				
XII.	Nov. 18th. 1899.	4,270,000	2,500	45	80.3	14	5	Mast cells, 6 per cent.

In eight of these twelve cases the leucocytes were markedly subnormal. In some of my cases (see following table) this abnormality is still more evident.

SPLENIC ANÆMIA.

	Age.	Sex.	Red cells.	White cells.	Hæmoglobin, per cent.	Remarks.
1	24	..	2,668,000	15,800	35	Polynuclears, 62.0 per cent. Lymphocytes, 36.0 " Eosinophiles, .4 " Myelocytes, 1.2 " Mast cells, 4.0 "

SPLENIC ANÆMIA (*Continued*).

	Age.	Sex.	Red cells.	White cells.	Hæmoglobin, per cent.	Remarks.
2	12	..	2,268,000	9,800	25	With neck glands. Polynuclears, 74.0 " Lymphocytes, 25.0 " Myelocytes, 1.0 " Normoblasts, = 4.0 (Count 500.)
			3,320,000	....	22	20 days later.
			3,436,000	....	25	56 " "
3	79	..	3,500,000	9,500	65	Diff. count 400 cells. Polynuclears, 60.0 per cent. Lymphocytes, 35.5 " Eosinophiles, 2.0 " Myelocytes, 2.5 "
4	26	..	3,634,000	8,600	60	March 9th. Polynuclears, 68.0 " Lymphocytes, 29.0 " Eosinophiles, 3.0 "
			3,968,000	12,800	60	March 19th. Polynuclears, 74.0 " Lymphocytes, 25.5 " Eosinophiles, .5 "
5	26	..	5,216,000	6,200	60	March 7th.
			5,157,000	4,700	60	" 9th.
				9,800	..	" 28th. Polynuclears, 74.0 " Lymphocytes, 24.5 " Eosinophiles, 1.5 "
6	36	..	3,300,000	3,500	45	July 22d.
			3,540,000	2,800	35	" 26th. Mitral and aortic regurgitation compensated.
7	13	..	4,280,000	2,100	42	Polynuclear, 59. per cent. Lymphocytes, 40. " Eosinophiles, 1. " No nucleated reds.
				1,300	48	7 days later.
			2,224,000	6,400	30	15 " " dying of hemorrhage.
8	18	..	384,000	1,800	35	Polynuclear, 55. per cent. Lymphocytes, 37.5 " Eosinophiles, 7.5 " No nucleated reds.
				1,900	45	8th day.
			4,024,000	1,450	35	12th day.
				1,500	..	15th day.
9	45	..	3,048,000	1,600	35	Polynuclear, 44. per cent. Lymphocytes, 55. " Eosinophiles, 1. " Two normoblasts. (Count 500 cells.)
10	17	..	2,560,000	700	20	July 21st.

SPLENIC ANÆMIA (*Continued*).

	Age.	Sex.	Red cells.	White cells.	Hæmoglobin, per cent.	Remarks.
				650	..	Repeated. Polynuclear, 66%. Lymphocytes, 33. per cent. Eosinophiles, 1. " (No nucleated in 150.)
				1,700	..	July 27th.
				900	..	July 31st.
			2,456,000	....	45	August 11th.
				2,200	40	August 20th.
			4,912,000	1,400	50	November 18th. Following July 5th, doing well.

Warthin has recently (*Trans. Assn. Am. Phys.*, 1903) called attention to the fact that in some cases of this type there is stenosis with calcification in the portal vein.

Hocke (*Berl. klin. Woch.*, April 21st, 1902) has reported with autopsy a case very similar in all respects to those of Osler (Banti's type). The blood showed:

Red cells.	Leucocytes.	Hæmoglobin,	Remarks.
3,750,000	3,200 to 5,800; near death.	7 grammes.	Lymphocytes greatly increased.

Yet Hocke considers it congenital lues!

PART II.

ACUTE INFECTIOUS DISEASES.

CHAPTER III.

INFLUENCE OF INFECTIOUS FEVERS ON THE BLOOD.

SOME of the blood changes found in acute infections are to be regarded as due simply to the fever associated with the disease. It is worth while, therefore, to consider what fever *per se* can do to the blood.

Maragliano[1] and others have shown that during fever from any cause a *contraction* of the peripheral vessels occurs. When fever disappears, whether spontaneously or from the action of antipyretics (phenacetin, quinine, etc.), a *dilatation* of the vessels follows.

Following the laws to which we have so often alluded, the contraction of the vessels causes a concentration of the blood with rise in specific gravity and in the number of blood cells per cubic millimetre. This concentration is still further increased by the greater loss of water which the organism suffers during fever than under normal conditions.

The effect of these two influences in increasing the number of red cells per cubic millimetre is, however, counteracted to a considerable extent by the sharing of the blood in the general tissue destruction which goes on with increased rapidity during fever. Many corpuscles are thus destroyed, but until the temperature falls the anæmia is covered up by the concentration. When the fever leaves the patient there is a sharp fall in the number of cells per cubic millimetre, due partly to the destruction of corpuscles (hitherto masked by concentration) and partly to the *dilution of the blood* which is the result of the post-febrile dilatation of the peripheral vessels above mentioned. The suddenness of this fall in the count is proportional to the suddenness of the fall in temperature.

The alkalinity of the blood has been often said to be diminished in fever, but recent research tends to show that these results were obtained by faulty technique, and it is doubtful whether the reaction of the blood shows any constant changes in fever.

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[1] Zeit. f. klin. Med., vols. xiv. and xvii.

Leucocytes and fibrin show no constant changes, though in the majority of infectious fevers they are increased. The tendency of the granules of polynuclear cells to lose or change their staining affinities in infectious disease has been noted by Ewing, Stengel, and Hirschfelt.

In the active stages of the great majority of infections the polynuclear cells become increased at the expense of the other forms and the eosinophiles become very scarce or disappear. In convalescence these changes are reversed, the polynuclears sink, the eosinophiles rise above normal, and for two or three months after the fever these latter conditions often persist in the blood.

PNEUMONIA.

The Blood as a Whole.

(*a*) Bacteriology.—The diplococcus lanceolatus has been repeatedly found in the blood of pneumonic patients, especially in those in whom there has been some secondary diplococcus infection (*e.g.*, diploccoccus endocarditis).

For example, Sittmann[1] out of 16 cases found diplococci in the blood of 6, most of which were complicated with lesions in other organs, and 4 of which were fatal, while of the 10 whose blood was sterile, 9 ended in recovery..

Boulay[2] found the organism in 2 cases shortly before death. Belfanti[3] found it but 6 times out of a large number of cases, and of these 6, 5 were fatal. Goldschneider[4] and Grawitz[5] got similar results. Cohn[6] in 32 cases found the organism in 9; 7 of these were fatal. The other 2 had empyema and other evidences of metastatic action of the pneumococci. White (*Jour. of Exp. Med.*, 1899, p. 425), in his very thorough study of 19 cases, got positive results in 3—all of which proved fatal, as did 7 of the 16 negative cases. Beco[1] studied 49 cases. Twenty of these ended fatally, and of these 20 there were 5 whose blood showed pneumococci by culture and 1 from which Friedländer's bacillus was cultivated. Out of 29 cases ending in recovery only 2 showed cocci in cultures from the blood. If large numbers of colonies can be cultivated from the peripheral blood, Beco considers the prognosis grave. A few colonies, however, are of no significance in prognosis. Fraenkel has obtained over 300 colonies from one puncture. Their virulence was less than that of those in the sputa, showing apparently the effects of the blood's antitoxic power. Nevertheless, it is probable that the presence of pneumococci in the blood is a bad prognostic sign. The most recent observations made with 5 to 10 c.c. of the blood well diluted in nutrient bouillon have shown a larger percentage of positive results. Thus Pieraccini[2] was successful in 11 out of 28 cases, and Silvestrini[3] in 15 out of 16, Berghini[4] and Prochaska[5] in almost every case, even the most favorable.

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[1] Deut. Archiv f. klin. Med., 1894, p. 323.

[2] Paris Thesis, 1891.

[3] Riforma Medica, Naples, 1890, No. 37.

[4] Deut. med. Woch., 1892, No. 414.

[5] Grawitz: Charité-Annalen, vol. xix.

[6] Cohn: Deut. med. Woch., 1897, No. 9.

(*b*) Coagulation is remarkably rapid, and in fresh specimens the fibrin network is very thick and appears within a few minutes, except in the rare cases with subnormal leucocytes. Here it may be absent or diminished.

(*c*) In cases with cyanosis the blood is often concentrated at the periphery so that its specific gravity is high and the number of corpuscles large.

(*d*) Monti and Berggrün[6] observed that in children the specific gravity was high throughout the course of the disease, falling with the temperature.

The toxicity of the blood is doubled (Albu: Virchow's *Archiv*, vol. cxlix.).

Red Cells.

During the fever the red cells are approximately normal (unless increased by cyanosis); but after the crisis there is often slight anæmia, and sometimes a severe one. The hæmoglobin is more markedly and more lastingly reduced than the number of red cells.

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[1] Beco: Revue de Méd., 1899, July 10th.

[2] Pieraccini: Centralbl. f. allg. Path., 1900, vol. xi., p. 470.

[3] Silvestrini: Centralbl. f. allg. Path., 1900, vol. xi., p. 447.

[4] Berghini: Ref. from Grawitz, p. 516.

[5] Prochaska: Deut. Arch. f. klin. Med., 1901, vol. lxx., p. 559.

[6] Arch. f. Kinderheilk., vol. xvii.

A more interesting and important observation was made by Türck in 1898, viz., that when the infection is severe or the patient of low vitality nucleated red cells (mostly normoblasts) may appear in the peripheral blood. In all Türck's cases megaloblasts as well as normoblasts occurred, but the latter were greatly in the majority. Dr. Badger and I studied a most interesting case of this type in 1898. The pneumonia ran a severe course and was followed by an empyema which proved fatal. The blood counts were made for the most part after the crisis. At autopsy the marrow of the femur was bright red from end to end. The blood showed the following:

Date.	Red cells.	White cells.	Haemoglobin, per cent.	Polynuclears, per cent.	Lymphocytes, per cent.	Eosinophiles, per cent.	Myelocytes, per cent.	Number of white cells counted.	Normoblasts.	Megaloblasts.
1898— January 13th	....	61,000	45	....	....	....	....	....	..	..
" 14th	....	71,500	..	90.0	7.0	....	3.0	600	22	4
" 15th	4,520,000	59,000	..	84.5	8.0	....	7.5	600	93	15
" 16th	....	51,800	..	84.5	12.8	0.2	2.5	600	54	4
" 17th	....	47,000	..	86.6	6.1	0.8	6.5	700	24	3
" 18th	....	26,700	..	87.2	10.0	....	2.5	500	?	?
" 19th	....	19,700	..	....	....	....	....	....	..	..
" 20th	....	25,000	..	92.5	7.5	....	....	400	3	..
" 21st	....	24,000	..	92.0	7.6	....	0.3	300	3	1
" 22d	....	......	..	87.0	12.5	0.25	0.25	400	..	..
" 24th	....	14,400	..	....	....	....	....	....	..	..
" 26th	....	19,100	..	....	....	....	....	....	..	..

Many of Türck's stimulation forms and many neutrophiles intermediate between myelocytes and polynuclear cells were seen.

Maragliano has noticed "degenerative" changes in the red cells in severe cases.

White Corpuscles.

1. Probably as early as the time of the chill, and certainly within a few hours after it, the leucocytes are greatly increased, and usually continue so throughout the febrile period.

2. There is no correspondence between the daily variations in temperature and the leucocyte curve. In cases in which a pseudo-crisis occurs (the temperature falling but rising again), the leucocyte count usually remains high, while at the time of the true crisis and often a few hours before it the leucocytes *begin* to fall. This fall, however, is hardly ever by "crisis," but though starting perhaps a little before the temperature, it is one to two days longer in reaching normal. When the temperature reaches normal by lysis the leucocytes fall with it, but generally more slowly, and reach normal later.

3. When resolution is delayed the leucocytosis continues, sometimes for weeks, and very gradually falls to normal in cases in which resolution eventually occurs without complication. If abscess, empyema, or gangrene follow, the leucocytes usually become still further increased.

4. The *degree of leucocytosis* is probably the resultant of the factors mentioned on page 97, and does not run parallel to the degree of fever or the amount of lung involved. Nevertheless, cases with extensive signs in both lungs, and especially those complicated by empyema or other suppuration, are more apt to have very high counts, provided the "reaction" of the patient against the infection is vigorous. Children have especially high count as a rule (see exception below). The cases appear to fall into the following groups as regards the degree of leucocytosis present:

1. Mild infection, vigorous reaction = slight leucocytosis.
2. Severe or moderate infection, vigorous reaction = marked leucocytosis.
3. Severe infection, feeble reaction = no leucocytosis.

(*a*) The patients in Class 1 all recover, but they are very few in number. (*b*) Those in Class 2, which includes over nine-tenths of all cases, may or may not recover, according as the fight between patient and disease comes out one way or the other.

(*c*) Those in Class 3 *almost invariably die*; there is not sufficient of a struggle to raise the leucocyte count. A striking exception to this rule is reported by Stockton (*Phil. Med. Jour.*, June 25th, 1898), a case of lobar pneumonia in a child of eight with three relapses and a total course of sixty-eight days. At the height of the second relapse the blood was examined and showed only 4,000 leucocytes per cubic millimetre. Of these there were 44 per cent of polymorphonuclear, 50 per cent small lymphocytes, 6 per cent large lymphocytes. In the second apyretic interval, sixteen days after the first examination, the count stood 7,840 leucocytes per cubic millimetre. Of these, 34 per cent were polymorphonuclear, 60 per cent small lymphocytes, and 20 per cent eosinophiles, 4 per cent large lymphocytes (?).

After the third seizure (three weeks later) the leucocytes were 10,080, with polymorphonuclear 45 per cent. Small lymphocytes 46 per cent, eosinophiles 8 per cent, large lymphocytes 1 per cent.

On the sixty-eighth day (in convalescence) the blood showed:

Red cells, 4,952,000; white cells, 7,600; hæmoglobin, 90 per cent. Polymorphonuclear, 57; small lymphocytes, 36; large lymphocytes, 2.5; eosinophiles, 4.5.

Very possibly this infection may have been due to some other organism than the diplococcus lanceolatus.

When either the patient or his disease *easily* gains the mastery there is no leucocytosis, or a very slight one; but in the much larger class of cases in which the struggle is a fierce one, leucocytosis appears, *whichever way the struggle results.*

Pick[1] noted that pneumonia complicating smallpox when the patients were already very sick, caused no leucocytosis, and the same is often true in those whose power of resistance is reduced by age, alcoholism, typhoid, or by some chronic disease.

Von Jaksch, noticing the fatality of cases without leucocytosis, suggested that we should induce leucocytosis by injecting turpentine or other irritants so as to cause abscess; but this has not proved of any benefit to the patient, nor has the production of leucocytosis without abscess, as can be done with pilocarpine or nuclein, been any more successful. There is no difficulty in producing the leucocytosis by these means, but all observers are agreed that it does the patients no good.

Leucocytosis is checked by antipyretics (Hare[2]) but not by cold bathing, which speaks in favor of the latter method of reducing temperature.

The general course of the leucocytes is seen in the accompanying charts from Billings, to whose excellent article I am greatly indebted.

Qualitative Changes.—As in most forms of leucocytosis, the polymorphonuclear leucocytes are enormously increased both absolutely and relatively, often making over eighty per cent of all the white cells.[3] Eosinophiles and blood plates disappear and the lymphocytes are absolutely and relatively much reduced. After the crisis this is reversed, the polymorphonuclear forms falling often below sixty per cent, while the eosinophiles and blood plates are above normal. The return of the eosinophiles to the circulation often occurs a day or two before the crisis. It seems to mean that the acme of the process has passed, and so constitutes a favorable sign in most cases. After the crisis the eosinophiles may run up to five to six per cent (300–450 absolute).

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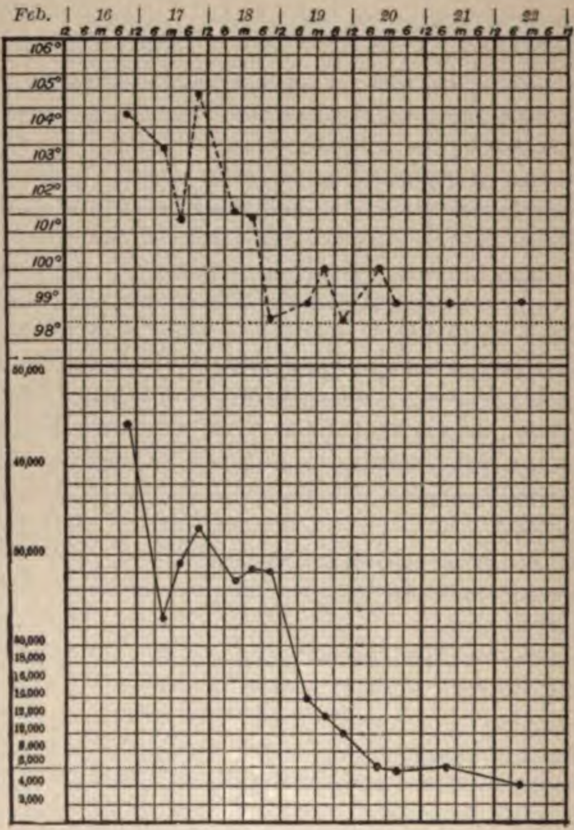
[1] Arch. f. Dermat. und Syph., vol. xxv., p. 63.

[2] New York Medical Record, May 9th, 1896.

[3] Löper believes that if the polynuclear cells make up from ninety to ninety-five per cent of all the leucocytes, the prognosis is very bad (Arch. de méd. exp., 1899, p. 724).

CHART I.—PNEUMONIA, SHOWING FALL BY CRISIS (BILLINGS).



The upper chart shows the course of the temperature, the lower that of the leucocytes.

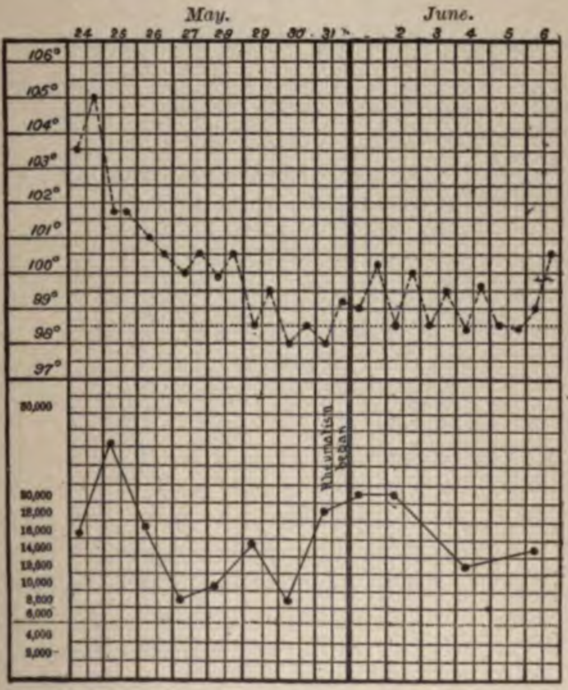
Myelocytes may be abundant (11.9 per cent or 1,056 absolute) and stimulation forms and transitional neutrophiles numerous. They have no known prognostic significance.

At and just after the crisis a great increase of blood plates takes place, gradually disappearing later.

As to the differential count in the (fatal) cases in which leucocytosis is absent, data are scanty. Bieganski thought the polymorphonuclear varieties decreased, Rieder found them increased, while Billings found them normal. No general law can be stated on this point as yet.[1]

In a case of bronchopneumonia complicating pertussis studied at the Massachusetts General Hospital in 1894, the conditions were entirely different from those just stated. The patient, a girl of six, had at entrance 72,100 leucocytes per cubic millimetre. Two days after the count was 94,600. A differential count made at the same time showed that the small lymphocytes made up 66 per cent of all

CHART II.—PNEUMONIA AND RHEUMATISM.



The upper chart shows the course of the temperature, the lower that of the leucocytes.

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[1] *Iodophilia* is present and marked in practically all cases. Dunn has noted that while in cases ending with crisis and resolution the reaction disappears in a day or two, it persists in those with delayed resolution.

the 94,600 leucocytes per cubic millimetre. The polymorphonuclear cells were reduced to 30 per cent. Lymphatic leukæmia was thought of, but the leucocytosis was gone in ten days, and within a fortnight the patient left the hospital well. In the light of recent studies in pertussis this is now explicable (see page 220).[1]

Diagnostic and Prognostic Value.

1. In cases of so-called "*central pneumonia*" in which the symptoms but not the physical signs of the disease are manifest, the presence of a well-marked leucocytosis is often of great diagnostic value. It excludes malaria, typhoid, and uncomplicated grippe as causes of fever, and if scarlet fever and suppuration can be excluded by other evidence, it makes pneumonia very probable.

I have repeatedly seen the diagnosis of pneumonia made in the absence of physical signs and largely on the evidence of the blood count, the diagnosis being confirmed several days later by the appearance of typical signs of consolidation. In a patient of Dr. F. C. Shattuck's, sick five days, yet showing no signs of consolidation of the lung, the presence of a marked leucocytosis excluded typhoid, the only other likely diagnosis, and led Dr. Shattuck to treat the case as pneumonia, the wisdom of which course was later demonstrated by the appearance of signs of consolidation.

2. Between pneumonia and capillary bronchitis the condition of the blood is of no help, as the latter also causes leucocytosis, and some cases affecting the larger tubes do the same.

3. In cases of pneumonia occurring in very old or very young people, in which the fever and symptoms may be very slight, the presence of leucocytosis may be the first thing to direct our attention to the lungs, dyspnœa and cough being absent.

In *prognosis*, the important point is that *the absence of leucocytosis is a very bad sign, while its presence is neither good nor bad.* It must be remembered also that in the very mildest cases we may find the same absence of leucocytosis which in any other but the mildest would be almost surely fatal.

This last point, which appears to me of great importance, is illustrated by the following figures:

Halla reported 14 cases; 2 had no leucocytosis, and both were fatal.

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[1] Stiènon: Jour. de Méd., de Chirurg. et de Pharm., Bruxelles, 1895, t. iv., fasc. 1.

Billings reported 22 cases; 1 had no leucocytosis and was fatal.

Laehr with 16 cases, and Rieder with 26, got similar results.

Ewing in 101 cases found leucocytosis absent in 6; 6 were fatal.

Von Jaksch and Kilodse likewise maintain that the absence of leucocytosis is usually fatal.

In our series 842 cases have been studied. In general they entirely confirm the results obtained by Billings and summarized above: 90 of them presented no leucocytosis at any time, and of these 83 were fatal; another one seemed moribund but finally recovered.

The evidence, therefore, is in favor of the view that when leucocytosis is persistently absent in any but the mildest cases the prognosis is almost fatal. *The presence of leucocytosis, on the other hand, is no guaranty whatever of a favorable issue.*

Reappearance of eosinophiles is a favorable sign in most cases. Indeed Becker (*Deut. med. Woch.*, 1900, p. 558) states that he has never found eosinophiles in fatal cases. The counts at the time of entering the hospital may be summarized as follows:

Cases with leucocytes under 10,000 = 90 (83 of these fatal)
" " " between 10,000 to 15,000 = 125
" " " " 15,000 " 20,000 = 192
" " " " 20,000 " 25,000 = 186
" " " " 25,000 " 30,000 = 114
" " " " 30,000 " 35,000 = 47
" " " " 35,000 " 40,000 = 44
" " " " 40,000 " 45,000 = 20
" " " " 45,000 " 50,000 = 10
" " " " 50,000 " 55,000 = 7
" " " " 55,000 " 60,000 = 2
" " " " 60,000 " 65,000 = 3
" " " " 65,000 " 70,000 = 1
" " " " 100,000 " 110,000 = 1
842

Bronchopneumonia.

In sixty-eight cases of bronchopneumonia recorded at the Massachusetts General Hospital, the following counts are recorded:

Counts.
Between 5,000 and 10,000 = 10
" 10,000 " 15,000 = 18
" 15,000 " 20,000 = 25
" 20,000 " 25,000 = 24
77

			Counts.
Between 25,000	"	30,000 =	9
" 30,000	"	35,000 =	8
" 35,000	"	40,000 =	1
" 40,000	"	45,000 =	2
" 45,000	"	50,000 =	2
" 50,000	"	55,000 =	1
" 100,000	"	185,000 =	3 (same case)
			103

The highest counts in this series were in a case of broncho- umonia in a baby of fifteen months. As the lymphocytes made he larger part of the increase, and as the cough came in parox- s with great cyanosis, pertussis was suspected. This case has ady been referred to on page 106, and a similar case is recorded page 193.

TYPHOID FEVER.

Bacteriology of the Blood.

Although it has long been known that the bacilli of Eberth could occasionally be found in the circulating blood or in the rose spots of typhoid cases, yet it is only within the last few years that such findings have been sufficiently constant to be of any practical value in diagnosis. The earlier investigators found the organism but seldom, probably because they used too small quantities both of blood and of nutrient bouillon. Using a larger amount of blood and diluting it well, it seems that bacilli can be found in the blood of most cases. Thus Busquet (*Presse Méd.*, June 21st, 1902) found them in all of 43 cases, generally at first examination.

Schottmüller (*Münch. med. Woch.*, September 23d, 1902) was successful in 182 out of 220 cases (82 per cent), occasionally in the first twenty-four hours, often by the fifth day, always in the second or third week. The bacilli were not found after normal temperature, but returned in relapse and recrudescence.

Neufelt,[1] Curschmann,[2] Scholz and Krause,[3] and Richardson[4] have succeeded in cultivating the bacilli from the rose spots in a total of 46 out of 56 cases.

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[1] Neufelt: Zeit. f. Hyg., xxx., 3, p. 499.

[2] Curschmann: Münch. med. Woch., 1899, p. 1597.

[3] Scholz and Krause: Zeit. f. klin. Med., 1900, vol. xli., p. 405.

[4] Richardson: Phil. Med. Jour., March 3d, 1900.

Quantitative Changes.

1. The *blood plates* are usually scanty, and the amount of *fibrin* is diminished. In one of Türck's cases, blood plates and fibrin were nearly absent, and a *hemorrhagic diathesis* developed. He considers a rapid falling off of the amount of fibrin and blood plates a bad prognostic sign, but in a case of hemorrhagic typhoid reported by Hamburger (Johns Hopkins Hospital Reports, vol. viii.) recovery took place, although the coagulation time was ten minutes.

2. Specific gravity follows the course of the hæmoglobin.

3. The general effects of fever (see page 186) are in part accountable for the changes next to be described, while some of them are more peculiar to typhoid fever.

Red Cells.

In Thayer's admirable study (Johns Hopkins Hospital Reports, vol. viii.) we find the following analysis of two hundred and sixty-five counts:

WEEKLY AVERAGE BASED ON ONE COUNT PER WEEK IN EACH CASE, THE AVERAGE BEING TAKEN FOR THE WEEK IN EVERY CASE IN WHICH MULTIPLE COUNTS WERE MADE.

1st	week	32	counts	4,913,312
2d	“	83	“	4,706,855
3d	“	54	“	4,555,814
4th	“	34	“	4,187,720
5th	“	22	“	4,118,590
6th	“	87	“	4,028,428
7th	“	8	“	3,309,125
8th	“	8	“	3,652,285
9th	“	6	“	3,509,666
10th	“	1	count	3,920,000
11th	“	1	“	2,109,333

All these counts refer to the febrile period of the disease.

Eighty counts were made *during convalescence.* The results were as follows:

ESTIMATES OF THE RED BLOOD CORPUSCLES DURING CONVALESCENCE ARRANGED ACCORDING TO THE PERIOD AFTER THE LAST DAY OF FEVER.

1st	week,	32	counts	4,540,000
2d	“	22	“	4,637,100
3d	“	15	“	4,252,000
4th	“	6	“	4,391,000
5th	“	2	“	5,469,000

Thayer comments: "It will be noticed that in the first week (of fever) the number of red blood corpuscles is already somewhat below the normal"—that is, taking the normal as from 5,500,000 to 6,000,000, as it seems proper to do in this country (see page 54).

From this point it steadily sinks week by week for the first nine weeks. After that the number of counts is too small to justify conclusions. The lowest point is probably reached about the end of defervescence in the majority of uncomplicated cases, yet when defervescence is slow, blood regeneration may begin well before the end of the febrile period. In the first two weeks of convalescence, regeneration is going on slowly. "After the second week, in addition to the fact that the estimates are but few, the results are vitiated by the fact that the cases remaining in the hospital at so late a period were for the most part instances of severe fever of long duration, after which, as is shown by the first table, a much greater degree of anæmia is reached" (Thayer).

SHOWING THE HIGHEST AND LOWEST COUNTS IN EACH WEEK.

		Highest.	Lowest.
1st	week	6,940,000	3,400,000
2d	"	6,604,000	2,240,000
3d	"	6,916,000	2,300,000
4th	"	5,884,000	1,426,000
5th	"	6,312,000	1,352,000
6th	"	4,904,000	2,014,000
7th	"	4,500,000	1,648,666

In only one of these cases could the high count be explained as a concentration of the blood through diarrhœa and vomiting, but counts made just after a bath are often very high owing to blood concentration.

Hæmoglobin.

Thayer's figures are as follows:

1st	week	of fever,	21	estimates	average	76	per cent.
2d	"	"	50	"	"	73	"
3d	"	"	32	"	"	67	"
4th	"	"	20	"	"	60	"
5th	"	"	15	"	"	58	"
6th	"	"	6	"	"	62	"
7th	"	"	4	"	"	50	"

Convalescence	1st	week,	22	estimates	average	67	per cent.
"	2d	"	19	"	"	69	"
"	3d	"	12	"	"	67	"

This table shows a gradual decline during the febrile period, with a very slow regeneration in convalescence. The hæmoglobin (as in most secondary anæmias) suffers more than the count of corpuscles, and is slower in reaching the normal, so that the color index is low throughout (see chart on page 201).

Leucocytes.

Thayer records 832 estimates of the white cells in uncomplicated cases.

Based on one count per week in each case, the average being taken for the week in every case in which multiple counts were made.

1st week of fever,	100 counts	6,400
2d " "	206 "	6,200
3d " "	150 "	5,700
4th " "	95 "	5,400
5th " "	58 "	5,380
6th " "	19 "	5,800
7th " "	13 "	6,300
8th " "	12 "	6,400

Thayer comments: "It would seem that the longer the disease lasts, the more profound the prostration, the lower the count." Ewing says: "The more severe the typhoid intoxication the lower the count." How great the variations may be even in the absence of any apparent complication is shown in the following table:

	Highest.	Lowest.
1st week of fever	15,000	1,600
2d " "	18,000	1,000
3d " "	13,000	1,000
4th " "	10,500	1,700
5th " "	10,500	2,300
6th " "	10,000	3,250
7th " "	11,000	4,000
8th " "	9,250	4,000
9th " "	9,300	2,000

Most of these high counts were in the blood of one individual, who, throughout the disease, without any apparent reason, showed constantly a large number of colorless corpuscles. The count of 18,000 may have been after a cold bath, which Thayer has previously shown often raises the count of white cells.

In convalescence the count of leucocytes begins to rise toward the normal as the following table indicates:

1st week of apyrexia,	32 counts.	6,000
2d " "	24 "	6,700
3d " "	16 "	6,800
4th " "	6 "	7,570

Thayer's results may be exhibited in the chart on the following page.

In the majority of the 1,357 cases recorded at the Massachusetts General Hospital, the course of the leucocytes from week to week has unfortunately not been followed with accuracy.

Most of our counts were made on the day of entrance to the hospital, presumably during the first or second week of the fever.

The range of the counts was as follows:

Between	1,000	and	2,000 =	13	cases.
"	2,000	"	3,000 =	62	"
"	3,000	"	4,000 =	171	"
"	4,000	"	5,000 =	230	"
"	5,000	"	6,000 =	224	"
"	6,000	"	7,000 =	217	"
"	7,000	"	8,000 =	150	"
"	8,000	"	9,000 =	118	"
"	9,000	"	10,000 =	81	"
"	10,000	"	11,000 =	43	"
"	11,000	"	12,000 =	27	"
"	12,000	"	13,000 =	12	"
"	13,000	"	14,000 =	6	"
"	14,000	"	15,000 =	3	"
				1,357	"

From these figures I have excluded all cases counted only under circumstances likely to concentrate the blood (cyanosis, after baths, after severe diarrhœa).

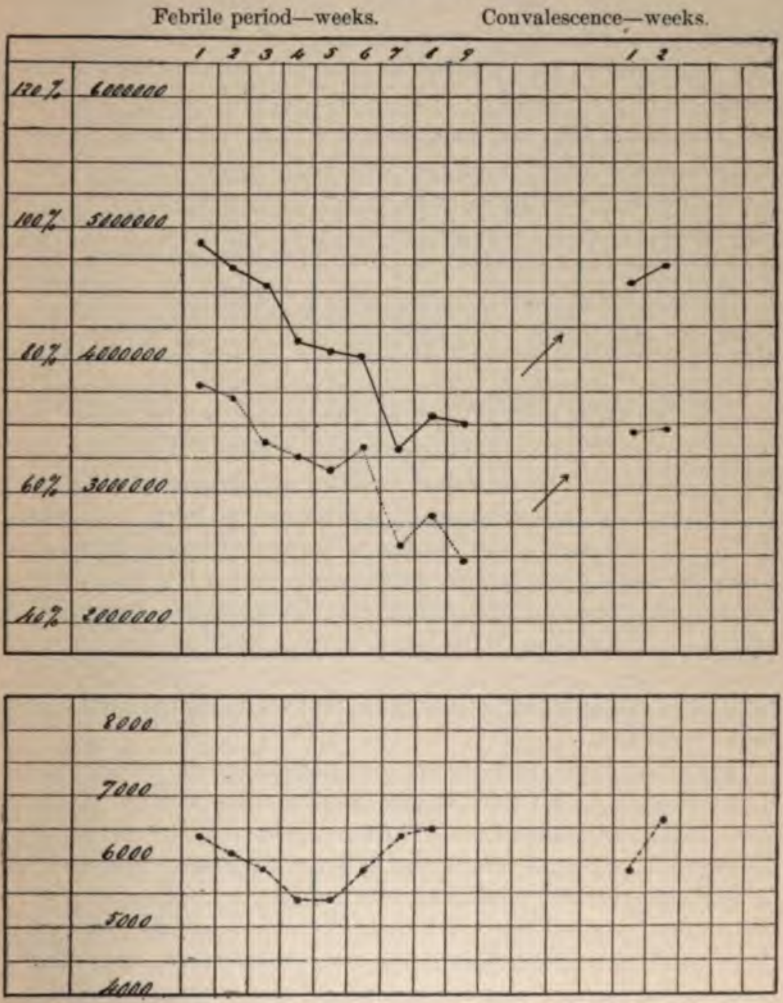
Of these cases 1,309, or 97 per cent, had less than 11,000 leucocytes per cubic millimetre at the time of entering the hospital, and 77 per cent had less than 7,000.

But these figures, like those reported by Thayer and Türck, differ from the reports of some other observers in not showing so large a proportion of very low counts. Thus Khetajurow expects to find only 2,500 to 3,000 leucocytes in the third and fourth weeks, but our observations show that this is not a law.

Complications.

Thayer's study of the effects of complications is by far the most thorough ever published.

CHART OF THE BLOOD IN TYPHOID FEVER.



Plain line = red cells. Dotted line = hæmoglobin. Broken line = white cells.

1. *Hemorrhage from the Bowels* (11 cases). The red cells fall off markedly in one case from 3,648,000 (eighteen days before) to

1,992,000, in another to 2,000,000; yet the first of these cases recovered.

The leucocytes showed no appreciable change in half of these cases, while in the rest there was some leucocytosis (24,800 in one case, 17,400 in another, 10,500 in a third), reaching its maximum in from twelve to twenty-four hours, and returning to normal in from two to seven days.

2. *Perforation of the Bowel* (8 cases). Leucocytosis was well marked in three (16,400, 23,400, and 16,000), slight in two (10,400 and 11,200), and completely absent in three, at the time of the perforation. Thayer studied the clinical features of these cases and the results of cultures made at operation, and concludes: "It is probable that slight local peritonitis always produces . . . leucocytosis unless the individual is already in a condition of profound general septicæmia. On the other hand, a sudden (general) infection of the peritoneum with large quantities of excessively malignant organisms may often result in complete absence of leucocytosis or a relatively slight rise, followed later by a fall. Three cases of streptococcus peritonitis showed no leucocytosis at any time. The prospect of relief by surgical interference is best in those cases with a leucocytosis." Thayer also shows that a preperforative leucocytosis due to local peritonitis about deep ulcers may occur. He adds, however, a summary of four cases in which symptoms suggesting perforation and accompanied by leucocytosis led to a laparotomy, yet in which no perforation was found, the symptoms being due in one case to thrombosis of the left iliac vein, while in the others no cause was found. In many of these cases the leucocytosis was very transitory, and without frequent (almost hourly) counts would have been overlooked.

In the series of cases of typhoid perforation reported by Shattuck, Warren, and Cobb (*Boston Medical and Surgical Journal*, June 28th, 1900) there are four cases of general peritonitis with no leucocytosis (3,800, 5,400, 7,300, and 8,000), and four cases with leucocytosis (14,000, 16,000, 17,200, and 23,000). Two cases with leucocytosis (14,300 and 13,200) showed at operation a perforation protected by local adhesions. In most of these only one count is recorded, so that the observations are of little value.

There is no doubt that leucocytosis *does* occasionally occur when no complication exists *so far as we can ascertain during life.* Four of the cases over 11,000 (see the above table) were counted repeatedly and complications were carefully sought for, but none were found. The most striking case showed the following counts:

October 3d	13,100
“ 4th	13,000
“ 5th	16,500
“ 7th	13,300
“ 8th	11,200
“ 10th	10,600
“ 13th	13,500
“ 15th	17,700
“ 17th	15,500, death; autopsy.

The autopsy showed typical typhoid lesions and nothing else.[1] Another and much milder case showed 11,000–12,000 white cells constantly for over two weeks, and no cause could be found to account for it.

In *typhoid septicæmia* with endocarditis but without intestinal lesions, Mayet and Bertrand (*Soc. Méd. d. Hôp.*, 1900, p. 996) report:

October 19th	13,800	with 91	per cent.	of	polynuclears.
“ 21st	14,800	“ 93	“	“	“
“ 23d	10,000	“ 91	“	“	“
“ 27th	18,900	“ 94	“	“	“

The typhoid bacillus was obtained in pure culture from the blood.

3. *Furunculosis.*—Thayer records 7 cases in all, of which the leucocyte count is very slightly raised *when we compare it with that usually found in typhoid* (*e.g.*, 9,000, 10,000, 10,200, 10,600, etc.).

4. *Thrombosis*—six cases in Thayer's study are of especial interest, because the leucocytosis with which each was associated appeared in three cases earlier than any of the localizing symptoms, such as pain and œdema.

The counts varied from 8,000 and 21,000 in femoral phlebitis to 24,800 in plugging of the iliac vein. I have had two similar cases.

5. *Pleurisy*—5 cases, all showed slight leucocytosis (10,000–12,000). Only in the purulent cases (empyema) was the count higher (23,000, 18,000). In one case the tapping revealed a bloody and purulent fluid containing only typhoid bacilli. After the tapping the leucocytes rose to 44,500.

In most of these cases the percentages of the different varieties of leucocytes was but little affected (*e.g.*, 68 per cent of polynuclear cells and 1.8 per cent of eosinophiles with a count of 23,000 leucocytes). This is *not* an ordinary leucocytosis

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[1] Thrombosis of internal veins and osteomyelitis were not carefully searched for at autopsy and may have existed.

6. *Pneumonia*—5 cases, 3 with leucocytosis, 2 without it (terminal infections). Both of those without leucocytosis and 2 of the others proved fatal. The counts were 35,000, 38,000, 8,200, 4,000 and 6,000. The neutrophiles were not increased as much as in ordinary leucocytosis. Türck records a case with but 1,600 leucocytes despite lobar pneumonia, and Kohler mentions several similar cases.

Bronchitis (*severe*) *and Bronchopneumonia*—4 cases, 3 showed leucocytosis (16,600, 17,200, 18,200).

8. *Periostitis*—3 cases with leucocytosis reaching 22,000, 17,600, and 13,000 (only 72 per cent of polynuclear cells in first case).

9. *Submaxillary Abscess* (streptococcus) with a maximum count of 18,200 which developed late in the course of the process. In another case with perforation peritonitis, the submaxillary abscess (staphylococcus and typhoid bacillus) did not produce any rise in the leucocytes.

10. *Otitis Media*—2 cases with leucocytosis of 15,600 and 11,800 (maximal). I have had 10 cases with maximal counts of 16,400, 14,000, 11,200.

11. *Parotitis*—3 cases, no leucocytosis in 2; in the other 30,500 (general infection with the staphylococcus aureus found at autopsy).

12. *Perirectal Abscess*—25,100 leucocytes. In one of my cases (moribund) a large ischio-rectal abscess developed without producing any leucocytosis.

13. *Pericarditis* (dry)—11,500 leucocytes.

14. *Bed-sores* (3)—16,000 leucocytes (average)

15. *Conjunctivitis*—9,330 leucocytes (polynuclear cells 74 per cent).

16. *Cholecystitis*—3 cases, all showing leucocytosis; 28,500, 21,200, and 14,400 (maximal).

17. *Cystitis*—3 cases, 1 with marked leucocytosis; 18,000.

18. *Urethritis*—3 cases, 1 with 13,700 leucocytes, of which 5.5 per cent were eosinophiles.

19. *Tuberculosis* (pulmonary)—1 case with 14,200 leucocytes, of which only 55 per cent were polynuclear. Türck records a similar case with a normal leucocyte count. Pregnancy and peripheral neuritis seemed to have no especial effect on the blood.

Qualitative Changes.

Red Corpuscles.—Türck notes "the relatively frequent presence of marked differences in the size of the red cells with very numerous dwarf forms; occasionally poikilocytosis and polychromatophilia," *i.e.*, the changes common to all varieties of secondary anæmia.

White Cells.—Thayer's extensive and painstaking studies are exhibited in the following table:

TABLE XII.

	Counts.	Polymorphonuclear neutrophiles, per cent.	Small mononuclear, per cent.	Large mononuclear, per cent.	Eosinophiles, per cent.
First week of fever....	12	74	13	12	0.5
Second " "	39	71	14	13	0.8
Third " "	34	66	21	11	0.3
Fourth " "	19	65	20	14	0.4
Fifth " "	8	62	18	19	0.3
Sixth " "	4	58	22	13	6.0†
First week apyrexia...	12	61	21	15	3.0
Second " " ...	7	49	31	17	2.3
Third " " ...	6	57	15	23	3.5

These averages, however, cover up some aberrant percentages. For example, there was one case which in the first week showed 15,000 leucocytes, of which 92 3 per cent were polymorphonuclear neutrophiles. No complication could be found. The lymphocytes were but 7.7 per cent, and the eosinophiles had altogether disappeared. Nine days after defervescence the leucocytes were 9,000, with 48.3 per cent of neutrophiles, 43.1 per cent lymphocytes, while the eosinophiles had risen to 8.6 per cent.

High percentages of polymorphonuclear neutrophiles sometimes occurred without an increase in the total count, *e.g.*, in the second week a case with 8,000 leucocytes, of which 94 4 per cent were polymorphonuclear, and in the third week a case with 4,000 leucocytes, of which 82 per cent were polymorphonuclear

In the ninth week one case showed 12 7 per cent of eosinophiles with 70.4 per cent of polymorphonuclear neutrophiles.

Summing up Thayer's observations, we find:

1. A steady diminution in the polymorphonuclears, the lowest

point being reached at the end of the pyrexia. This is an absolute diminution.

2 A relative increase in the lymphocytes, especially the larger forms; absolutely their number is not much changed.

3 A reduction (relative and absolute) of the eosinophilic cells during the pyrexia followed by an increase in convalescence, which may amount to a considerable eosinophilia.

Türck's results are practically the same. He adds that eosinophiles may actually disappear from the blood at the height of the disease, and considers that their reappearance or increase previous to defervescence augurs a relatively short course for the fever, and (aside from the occurrence of complications) a good prognosis. Myelocytes and *Reizungsformen* were occasionally present in his preparations, even in a case with a leucopenia of 4,200 and but 52 per cent of polymorphonuclear neutrophiles.

Naegeli (*Deut. Arch. f. klin. Med.*, vol. lxvii., p. 279) has made a most careful study of fifty cases with fifteen to twenty observations in each. His conclusions are:

I. In the first week, during the "step-ladder" ascent of fever, there may be a slight polynuclear leucocytosis.

II. The second and third weeks are characterized by leucopenia, with a marked diminution of polynuclears, slight diminution of lymphocytes, and *absence of eosinophiles.*

III. In the "period of steep curves" eosinophiles reappear, lymphocytes increase.

IV. Convalescence: Polynuclears reach their minimum while lymphocytes and eosinophiles rise above normal. It takes about two months for the blood to return to normal. All these changes are more marked in children. Naegeli considers the eosinophiles of importance in prognosis, and considers that in complications the polynuclears should rise. If they do not the prognosis is poor.

Kölner (*Deut. Arch. f. klin. Med.*, 1898, vol. xl., p. 221) found that in cases complicated by pneumonia or otitis, the leucocytes were sometimes increased and sometimes diminished.

Iodophilia occurs in a small proportion of the polynuclear cells at some time during the course of most cases of typhoid fever, especially on the second and third weeks.

Summary.

1. The red cells suffer to the extent of about 1,000,000 in the course of an average case, the reduction taking place gradually, and being most marked at the end of defervescence in most cases Sweating, vomiting, or diarrhœa may cause considerable transient elevation in the count of red cells, while sudden losses follow intestinal hemorrhage. Occasionally a very severe post-febrile anæmia occurs, the red cells being reduced nearly to 1,000,000 with the qualitative changes of a grave secondary anæmia. In most cases the qualitative changes are slight.

2. Hæmoglobin, as in most cases of anæmias, suffers somewhat more than the number of red cells.

3. The number of leucocytes is subnormal throughout the disease, averaging about 5,000 at its height, though much lower figures are common. This leucopenia progresses with the severity and duration of the infection. Cold baths cause an immediate transient increase in the number of leucocytes in the peripheral circulation, an increase which may amount to double or triple the number before the bath.

Differential counts show, during the febrile period, a progressive diminution in the number and percentage of the polynuclear cells, with a corresponding rise in the percentage of lymphocytes and large mononuclear cells, and a great diminution or even disappearance of the eosinophiles. In convalescence the percentage of eosinophiles markedly increases, often before the other forms have resumed their normal numbers.

4. Most complications, especially inflammations, produce a leucocytosis, but a particularly malignant infection may be followed by no increase and even by a diminution in the number of leucocytes. In many of the leucocytoses following complications the percentage of polymorphonuclear cells does not rise.

Diagnostic Value.

There are few diseases (outside of those known as diseases of the blood itself) in which the blood count is so often of value in diagnosis. The diagnosis of typhoid fever is made by exclusion—exclusion of other causes of fever and of local inflammatory processes in particular.

1 In this process of exclusion the blood is a most powerful adjuvant, inasmuch as almost all *local inflammatory processes have leucocytosis, while typhoid* (uncomplicated) *does not.* I recall two cases in which the chart and symptoms pointed to typhoid, but in which the persistent marked leucocytosis directed attention to the search for an inflammatory focus. Both were at first unattended with pain, tenderness, or other localizing symptom, but later signs and symptoms began to point to the *liver*, from which pus was evacuated by puncture. These cases of *abscesses of the liver* are typical of the value of blood examination for any deep-seated suppuration. I have seen good clinicians puzzled for twenty-four hours over the diagnosis between appendicitis and typhoid, but the indication of the blood count was always fulfilled. Pyæmic or septicæmic processes are usually distinguishable from typhoid by the same test—the presence of leucocytosis in the former.

Of the value of the blood in distinguishing certain cases of pneumonia from typhoid I have already spoken on page 194.

2. Aside from local or general pyogenic infections perhaps the disease most often confounded with typhoid is *malaria.* This is especially the case in the southern part of this country, where for want of proper blood examination the confusion of the two diseases is indicated in such a term as "typhomalarial fever." Malaria and typhoid are alike in having no leucocytosis, but the presence of the malarial parasite is an absolute test and in marked cases is always decisive. Very mild cases of malaria may show so few organisms in the peripheral circulation that without prolonged search they cannot be found, and in the severest types of all the organisms are not very abundant. In the vast majority of cases, however, the organism can be readily found and our diagnosis made certain.

3. *Tuberculosis*, local or miliary, if uncomplicated by any pyogenic organisms, cannot be distinguished from typhoid by the blood count alone, as neither disease shows leucocytosis, but here the Widal reaction (see page 529) comes to our rescue.

A large proportion of lymphocytes is commoner in typhoid than in tuberculosis, but it may occur in either disease. In the majority of cases, however, tuberculosis is complicated with septicæmia from a secondary pyogenic infection, and is then easily distinguished by the existence of leucocytosis.

4. *Typhus fever* has not been well studied and the reports of its blood condition are contradictory. At present we cannot say

whether or not it can be distinguished from typhoid by the blood examination. In most cases the absence of a serum reaction will exclude typhus.

5. Two cases of erythema nodosum with fever between 101° and 103° gave me trouble in diagnosis lately. In both the blood was normal and differed from typhoid only by the absence of a serum reaction. Thayer has reported a similar case (*loc. cit.*, p. 530), in which, however, there was a marked leucocytosis throughout.

6. *Trichiniasis* may run a course quite indistinguishable clinically from that of typhoid, but the presence in trichiniasis of a leucocytosis with marked eosinophilia and the absence of Widal's reaction will decide any case of doubt.

7. Most auto-intoxications (ptomaine poisoning) produce leucocytosis, and can therefore be distinguished from typhoid.

8. *Meningitis*, especially in its epidemic cerebro-spinal form, has many symptoms like those of typhoid, but it always produces leucocytosis, and is never associated with Widal's serum reaction.

9. From *influenza* typhoid cannot be distinguished by the blood count, as neither of them produces leucocytosis. Here the blood gives aid only through the serum reaction.

10. *Acute Infectious Dysentery* may present (especially in the tropics) many features that remind us of typhoid. As a rule it produces no leucocytosis, but it is distinguishable from typhoid by the presence of Widal's reaction in the latter.

The occurrence of complications in typhoid may mask its characteristic blood changes so as to make the blood useless in diagnosis; but in most early cases, in which the diagnosis is especially important and difficult, the blood shows no leucocytosis and is therefore of great value in the exclusion of other diseases.

Prognosis.

In prognosis Naegeli (*loc. cit.*) agrees with Türck in regarding the persistence or early reappearance of eosinophiles as a favorable sign, and believes that a normal number of polynuclear cells is a good sign when the outlook is more serious, if the leucocyte count is very low and does not increase during complications.

DIPHTHERIA.

Bacilli of diphtheria in the circulating blood are practically never to be found.

The specific gravity, according to Grawitz, is *above* normal at the height of the disease. He obtained the same result experimentally by injecting cultures of the Klebs-Löffler bacillus into dogs and rabbits. He concludes that the poison of the disease is lymphagogic and so concentrates the blood.

Red Corpuscles.—Morse's[1] investigations show an average of 5,100,000 in twenty cases counted during the first week of the disease and of 5,150,000 in 10 cases during the second and third week of the disease—practically normal figures.

These are the first systematic[2] investigations of the red cells in diphtheria and are confirmed by the reports of Ewing, Engel, and Billings. The latter observer in counts made in seven cases during the first five days of illness found an average of 5,600,000 + red cells per cubic millimetre. During the first five to ten days after this, the same cases showed an average loss of 510,000 cells per cubic millimetre; five out of the seven showing considerable losses, two remaining about the same. These were cases treated without antitoxin. The two cases showing no loss of red cells were both very mild, one having no membrane at any time. The diminution ranged from 470,000 (third day) to 2,040,000 (sixth day). As a rule no diminution can be made out until after the third or fourth day.

Out of twenty-three cases treated with antitoxin and each counted several times over, only three showed any considerable diminution in the red cells and these lost less than 400,000 each, not much beyond the limit of error (200,000) allowed for by the investigator, and all of them severe cases. Six patients who were anæmic when admitted (average = 4,640,000) showed a steady *rise* in the red cells as the disease (treated with antitoxin) progressed.

It is evident from these figures that antitoxin largely prevents the anæmia which usually develops in the first five to ten days. In cases not treated with antitoxin the regeneration from the resulting anæmia is slow. Healthy individuals injected with antitoxin showed a very moderate reduction in the red cells in about one-half the cases, the greatest loss being 932,000 per cubic millimetre (fifteen cases counted by Billings).

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[1] Boston Medical and Surgical Journal, March 7th, 1895.

[2] Earlier reports are faulty as to technique.

Qualitative Changes.—Billings' careful study of stained specimens showed no deformities in size or shape and no nucleated red cells, but Engel has found normoblasts. Polychromatophilic red corpuscles were very few in the cases in which antitoxin was used, but more numerous when it was not used.

Hæmoglobin.—Here again the most thorough investigations are those of Billings. In cases treated without antitoxin there was an average loss of ten per cent, regained in part during convalescence, but as usual reaching normal later than the count of corpuscles. When antitoxin was given, the diminution of hæmoglobin was less marked, but when the decrease did occur the return to normal was slow compared to that of the red cells, even when the patients were up and about and apparently well.

White Corpuscles.—Leaving out the older observations in which the technique was probably faulty, the principal investigators are Morse, Ewing, Gabritschewsky, Billings, Filé, and Engel.

All agree that a considerable leucocytosis is present in most cases—34 out of 36 of Billings' cases, 26 out of 30 of Morse's (the latter made but one count in each case), 49 out of 53 of Ewing's. In a general way, the severest cases show the greatest leucocytosis, but it does not follow the pulse, temperature, nor the extent of the membrane, and "the ordinary clinical examination of the patient is of much greater value in . . . prognosis . . . than any information to be gained from the examination of the blood. The latter is simply confirmatory, never indispensable" (Billings). Morse's conclusions are the same, although he considers that with notable exceptions the amount of membrane is a rough measure of the degree of leucocytosis. He finds no correspondence between the glandular swellings and the degree of leucocytosis, though he noted that "in the fatal 'septic' cases with greatly enlarged glands," very high counts were present. Other cases with little or no enlargement of glands showed equally high counts, however.

Ewing's 4 cases without leucocytosis were all mild, but of Billings' 2 cases without leucocytosis one was the severest of his whole series, while the other was mild. Of Morse's 4 cases without leucocytosis 3 were mild and 1 was severe. Gabritschewsky's 14 cases all showed leucocytosis.

Putting the results of these four observers together we see that when leucocytosis is absent the cases are *either* very mild or very severe, conditions analogous to those to be noted in pneumonia and septicæmia The counts in recent epidemics range from normal to 48,000 (Morse) or to 38,600 (Billings). Felsenthal[1] found 148,229 per cubic millimetre in one case, and Bouchut's[2] counts are often over 75,000.

In a general way the counts rise while the disease progresses and fall gradually as improvement goes on, disappearing after the membrane. "The leucocytosis is well marked by the third day and very likely earlier" (Morse). Billings found an increase after one day's illness, but usually less than was present later in the disease; one of his cases, however, had a higher count on the first day of the disease than on any subsequent day, though no antitoxin was given.

The injection of antitoxin has apparently no effect upon the leucocyte (strange to say) except in the first twenty-four hours after its use. Immediately—*i.e.*, within thirty minutes after an injection—the leucocytes are stated by Ewing to be considerably diminished, but the leucocyte curve does not reach normal any sooner than in cases in which no antitoxin is given, although it begins to fall in the majority of cases after the injection. The same thing (according to Billings) takes place without antitoxin.

The leucocytes of healthy persons are likewise unaffected by antitoxin injections.

Qualitative Changes.—All authors agree that in most cases the neutrophiles are increased. Morse found an average of 80 per cent in 26 of his 30 cases. Of the other 4, 1 was normal and 3 were subnormal (58, 59, and 59 per cent); 2 of these were convalescent, the other had been sick a week and had 12,000 white cells per cubic millimetre. A marked lymphocytosis was present in 2 of Ewing's 53 cases, 43,200, and 13,950 absolute.[3] In Billings' cases the polymorphonuclear varieties averaged 80 per cent and the lymphocytes 19 per cent, the eosinophiles being reduced to 1 per cent on the average and often being entirely absent. With Morse eosinophiles averaged 2 per cent.

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[1] Archiv f. Kinderheilk., vol. xv., p. 78, 1893.

[2] Comptes Rendus, 1877, lxxv., No. 3.

[3] In a case of Rieder's, aged three years, the lymphocytes rose from 19 per cent during the fever to 64 per cent in convalescence.

The proportion of polymorphonuclear cells is usually directly proportional to the total increase of leucocytes.

Ewing thinks that "the staining reaction of the leucocytes is an accurate measure of the severity of the diphtheritic infection," and this staining reaction he finds increased in favorable cases by the injection of antitoxin.

Billings did not find any such changes in "staining reaction," though he claims to have carefully followed out Ewing's procedures.

Pitkianen (*Gaz. clin. de Botkin*, 1901, p. 1033) states that in unfavorable cases the eosinophiles disappear by the third or fourth day, and the percentage of polynuclears is persistently elevated. If the eosinophiles are constantly to be found, the prognosis is good. In convalescence they rise above normal. He contrasts the presence and steady increase of these cells in scarlatina with their diminution in diphtheria (until convalescence) and considers the difference to be of diagnostic value.

Engel[1] found that antitoxin at first slightly increased the percentage of lymphocytes, and sometimes this increase was very marked. In one case the lymphocytes increased from 24 to 65 per cent after antitoxin.

The point on which he specially insists is the presence of considerable numbers of *myelocytes* in fatal cases.

Of the patients examined by him 17 died, and 9 of these had from 36 to 168 myelocytes in every one thousand leucocytes. Myelocytes were also present in some of the patients who recovered, but in smaller numbers (1.3 to 1.5 per cent).

In one case he found on the third day of the disease 4.3 per cent of myelocytes, and from this point the percentage gradually rose to 13.8 per cent, and then fell, there being 1.7 per cent present at the time of death. An abscess occurring in the case showed only the usual polymorphonuclear leucocytes in its contents. He concluded that a large percentage of myelocytes is a bad prognostic sign in any case.

Myelocytes are not mentioned in any of the numerous differential counts made by Gabritschewsky, Ewing, Morse, and Billings, so that Engel's observation is so far unique.

Iodophilia is usually present.

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[1] Gesellsch. f. innere Med., Berlin, July 6th, 1896.

Summary.

1. Moderate anæmia, especially in cases treated without antitoxin. Regeneration is slow.

2. Leucocytosis, very roughly parallel to the severity of the disease, unaffected by antitoxin treatment, gradually decreasing as the disease passes off, sometimes absent in very mild or very severe cases.

3. Polymorphonuclear leucocytes much increased during febrile stages, often diminished in convalescence.

4. Myelocytes numerous in some severe cases.

The blood examination has no diagnostic value so far as I can see; in prognosis the absence of leucocytosis (except in obviously mild cases) and the presence of many myelocytes are apparently bad signs.

CHAPTER IV.

ACUTE INFECTIOUS DISEASES (CONTINUED).

SCARLET FEVER.

Heubner[1] noted hæmoglobinæmia in one case. Fibrin is not increased even at the height of the fever, provided inflammatory complications are absent.

Red Cells.—Very little is to be found in literature upon the subject. Kotschetkoff[2] noted a gradual diminution of the red cells to about 3,000,000, regeneration taking place in the course of not less than six weeks. Other observers have found little or no anæmia.

Hayem[3] estimates the average loss of red cells at 1,000,000. In mild cases he finds the lowest figures on the first day of normal temperature. In severer cases in which the fever comes down slowly, the red cells may not reach their minimum till twenty-four hours after the normal temperature is regained.

Felsenthal[4] in six cases found the count to be 4,500,000 to 5,500,000—no considerable variation from normal.

Zappert[5] in six cases found it to be from 3,920,000 to 4,500,000, an average of 4,150,000. Normoblasts are occasionally seen—as in one of Türck's cases, and the normal variations in size and shape are exaggerated.

White Cells.—Most observers are agreed that *leucocytosis is the rule*, contrasting in this respect with measles, in which no leucocytosis occurs. The increase attains its maximum two or three days after the eruption. In light cases it may sink to normal even before the fever is gone, while in severer cases it may persist *several days after normal temperature is reached.* Von Limbeck had a case in which the leucocytosis persisted for twelve days after the temperature had become normal. Forty thousand per cubic millimetre is not unusual in well-marked cases. Rieder's ten cases averaged 17,500; Felsenthal's six counts were between 18,000 and 30,000. My own are similar.

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[1] Deut. Arch. f. klin. Med., vol. xxiii.

[2] Ref. in Petersburg. med. Woch., 1892, 1.

[3] *Loc. cit.*, p. 914.

[4] Arch. f. Kinderheilk., 1892, p. 80.

[5] Zeit. f. klin. Med., 1893, p. 292.

In a general way the severest cases are apt to have the highest leucocyte counts; the figures have no direct relation to the amount of fever, glandular swelling, or to complications in the ear or kidney.

Van den Berg (*Archiv für Kinderheilk.*, 1898, vol. xxv., p. 321) in 12 cases found the red cells in uncomplicated cases usually above 4,000,000. Endocarditis or nephritis, he found, reduces the erythrocytes and hæmoglobin very rapidly, and in some cases as low as 2,000,000 with 25 per cent hæmoglobin.

The leucocytes averaged about 17,000, but 2 cases exceeded 30,000; the increase lasted from twenty to thirty days.

Mackie (*Lancet*, 1901, vol. ii., p. 525) found leucocytosis in each of 25 cases, one case reaching 93,300; but in no case was the leucocytosis present until the day after the appearance of the rash.

Rechzeh (*Zeit. f. klin. Med.*, 1902, p. 107) studied ten cases and noticed as a rule no changes in the number of red cells nor in the hæmoglobin. Poikilocytosis and erythroblasts were occasionally noticed. The leucocytosis he found to run parallel with the fever curve, reaching the highest figures when the rash was at its worst, and then rapidly falling.

Regarding the percentages of the different leucocytes he confirms the findings of earlier writers.

Sacquépée (*Arch. f. Méd. Exp.*, 1902, p. 101) made 50 counts in 14 cases and reached the following conclusions:

1. About the third day of the illness there is a marked and sudden rise in the absolute and relative number of polynuclear with a slight absolute increase of lymphocytes. This raises the total leucocyte count often to 20,000, once to 31,000; 85 to 90 per cent of this increase is made up by the polynuclears. This increase rarely lasts beyond the seventh day, and by the twentieth day the total count is generally subnormal. There is no parallelism between the count and the severity of the disease.

2. Beginning about the fourth day, there is an eosinophilia (highest, 13 per cent or 1,950 per cubic millimetre) which falls very slowly so that even in the third or fourth week the eosinophiles are above normal.

3. In the second week there is a slight absolute increase of lymphocytes.

4. Streptococcus complications raise the number of polynuclear cells and depress the eosinophile count.

Qualitative Changes.—The polymorphonuclear forms are increased, often to ninety per cent, soon falling except in the worst cases. The peculiar characteristic of the disease is the persistence of eosinophiles in all but the severest cases despite the increase of polymorphonuclear forms. The only other infections of which this is true are tetanus and acute articular rheumatism. They may run as high as five per cent during the fever, and are still more numerous in convalescence, remaining increased for six weeks. According to Kotschetkoff, disappearance of eosinophiles is a bad prognostic sign except at the very beginning of the fever, when they may be temporarily absent in favorable cases. Presumably they have some connection with the exanthem, eosinophilia being so common in connection with skin lesions. They may number 15 to 20 per cent of the leucocytes in convalescence (Bensaude). Türck reports 14.3 per cent (1,800 absolute) in one case and 13.3 (800 absolute) in another. Felsenthal's average is 5 per cent; Zappert's, 3 per cent. The lymphocytes are decreased proportionately to the severity of the case, the worst cases showing only 2 to 4 per cent.

An increase of eosinophiles during a scarlatinal nephritis is regarded by Neusser and his pupils as a favorable sign, and their absence as ominous. In ordinary cases without nephritis they reach their maximum in the second or third week and are not normal till the sixth. In the active stages of the disease myelocytes, transitional neutrophiles, and "stimulation forms" occur.

Summary.

Slight anæmia.

Leucocytosis beginning just after the eruption and often lasting about a week.

Eosinophiles increased from the fourth day until late in convalescence.

Diagnostic and Prognostic Value.

1. The chief importance of the blood examination is in distinguishing the disease from measles and the eruptions of other diseases. Measles has no leucocytosis.

2. Whether the prognostic significance attached by Neusser and others to the percentage of eosinophiles is genuine or not, cannot as yet be positively stated.

MEASLES.

In mild cases the blood shows no changes at all. When bronchitis, coryza, and conjunctivitis are very marked, fibrin may be increased.

Red Cells.—In mild cases no change—never over 400,000 or 500,000 red cells are lost (Hayem). Felsenthal's eight cases showed counts of 5,000,000 to 5,500,000.

White Cells.—There is no leucocytosis, often a leucopenia during the eruptive stage. In convalescence the lymphocytes and especially the large mononuclear forms are increased. Felsenthal in eight cases found the count normal or diminished. Pée found but 4,000 in a case with a fever of 102.7°. Rieder's eight cases averaged 7,500, being *lowest* at the height of the disease and increasing as fever passed off. Complication with catarrhal pneumonia or a very bad bronchitis and coryza, may slightly raise the count. The eosinophiles, contrary to the example of scarlet fever, are often diminished during fever.

Combe (*Arch. de Méd. d. Enf.*, 1895, vol. ii., p. 345) found in the incubation (never later) a polynuclear leucocytosis. As the rash appears this leucocytosis disappears and leucopenia takes its place.

Plantenga (*ibidem*, March, 1903) confirms these findings in twenty-nine cases. A "distinct and constant leucocytosis" occurring in incubation and rising as high as 20,000 with 75 per cent of polynuclear cells gives way to leucopenia when the rash comes out. The eosinophiles are diminished or absent during the fever.

Renaud (*Thèse de Lausanne*, March, 1900) also confirms Combe's findings and thinks the pre-eruptive leucocytosis of diagnostic value. This increase and the subsequent decrease concern wholly the polynuclear cells. He generalizes from six cases.

Courmont studied also six cases (*Gaz. des Hôp.*, 1901, p. 1001) and agrees in the main with Renaud but finds some polynucleosis in the eruptive stage. Myelocytes (he agrees with Weil) are absent. In measles occurring in adults Courmont finds a slight polynuclear leucocytosis at the outset, and in this he agrees with Weil (*Thèse de Paris*," 1900, four cases).

Rechzeh (*loc. cit.*) in ten cases got practically similar results, and was struck with the fact that the blood presents a picture almost the opposite of that in scarlatina.

Tileston (*Boston Med. and Surg. Jour.*, 1904) in twenty-five cases found no leucocytosis in the prodromal or eruptive stages, though the percentage of polynuclear cells was usually increased. Later this increase was replaced by a slight increase in the lymphocytes. Eosinophiles and blood plates were diminished until convalescence, when the former became normal or slightly increased. All complications produced leucocytosis, and in every case the occurrence of leucocytosis could be explained by a complication.

The Massachusetts General Hospital records furnish the following counts in eleven cases:

TABLE XIII.—MEASLES.

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
4	..	....	11,000	..	Rash out; temp. 104°.
11	..	....	10,100	..	
38	M.	4,700,000	9,000	65	"Black measles"; petechiæ.
8	M.	....	9,000	..	Differential count normal.
21	..	....	8,200	..	Rash out; temp. 103°.
23	F.	....	8,000	68	104°; eruption out.
4	M.	5,000,000	7,000	60	Eruption just out.
10	M.	....	6,000	..	103°; three days before the eruption; differential count normal.
			6,000	..	Eruption out one day.
			6,000	..	Eruption out three days.
53	F.	....	3,500		
33	F.	....	3,500	67	
14	..	....	1,400	..	

The *value* of the blood examination is considerable in excluding scarlet fever, diphtheria, and syphilitic roseola, all of which show leucocytosis. It cannot apparently be distinguished by the blood count from *rötheln* (German measles).

RÖTHELN (GERMAN MEASLES).

Plantenga (*loc. cit.*) in nine cases found the blood like that of measles. I have seen two cases with 6,000 and 8,000 leucocytes, respectively.

MUMPS.

Seven cases of *mumps* under my care showed no leucocytosis. One case with orchitis showed 19,400 leucocytes and 90 per cent hæmoglobin on July 1st; 14,600 leucocytes on July 3d, and 17,000 July 5th.

Sacquépée (*loc. cit.*) records 30 counts in 15 cases. At the beginning of the disease he finds in about one-half the cases a slight increase in the total count (highest 13,600) 10 cases had never more than 12,000. The increase is largely in the lymphocytes. The polynuclears averaged 54 per cent, and in 2 cases were 16 per cent and 25 per cent, respectively. The eosinophiles averaged 0.7 per cent (subnormal). In 5 cases with orchitis he found a polynuclear leucocytosis (10,000 to 18,000).

WHOOPING-COUGH.

Meunier (*Archives d. Maladies de l'Enfance*, April, 1898) reported studies in 102 cases of whooping-cough. Lymphocytosis is early and constant. The counts average 22,700 in the cases examined during the catarrhal stage and before the advent of typical "whooping" paroxysms. In the paroxysmal stage the leucocytes average 40,000—the maximum being 51,250. In infants under four years the leucocytosis is far more intense than in older children. After the fourth year the count runs from 12,000 to 18,000. All the varieties of leucocytes are increased, but the lymphocytes are relatively as well as absolutely increased—a true lymphocytosis perhaps due to stimulation of the bronchial lymph glands. The increase begins in the earliest stages of the disease before the cough begins and persists into convalescence.

Meunier found no such changes in the blood of cases of bronchitis or tracheitis, and suggests that the blood count may be of use in the investigation of doubtful epidemics in schools or hospitals. Cima (*Pedriatria*, 1899, No. 9), Stengel and White (*Univ. Penn. Med. Bull.*, November, 1901, and De Amicis and Pacchioni (*Clin. Medica*, 1899, vol. iv., p. 103) confirm these observations, though in their cases the average lymphocytosis was somewhat less—17,900.

The following cases exemplify these rules (see also page 193).

TABLE XIV.—WHOOPING-COUGH.

Age.	Red cells.	White cells.	Per cent hæmoglobin.	
3	5,192,000	75,000	47	July 23d. Polynuclear, 42. Lymphocytes, 57. Eosinophiles, 1.
	....	26,500	....	August 19th.
				August 31st. Polynuclear, 56. Lymphocytes, 43. Eosinophiles, 1.
5		32,800		Lymphocytes, 69.

Steven (*Lancet*, vol. xx., 1902) reports a case of "broncho-pneumonia" with paroxysms of convulsive cough and cyanosis. The blood count is remarkable, but points, I think, to pertussis as the most probable diagnosis. I have seen two similar cases (see pages 193 and 106). Stevens' figures are as follows: Red cells, 4,800,000; hæmoglobin, 100 per cent; leucocytes, 236,000. Of these there were: Polynuclears, 33.6 per cent; small lymphocytes 50.2 per cent; large mononuclear, 15.2 per cent; eosinophiles, 1 per cent.

VACCINATION AND VACCINA.

Billings[1] and Sobotka[2] found leucocytosis reaching its height (15,000) with the maturity of the vaccine pustule, and composed chiefly of polynuclear cells; but in adults' blood Courmont and Montagnard[3] found nothing abnormal after vaccination.

In generalized *vaccinia* Enriquez and Sicard[4] found the blood normal.

SMALLPOX (VARIOLA).

Red Cells.—According to Hayem no other fever is so destructive of red cells. During the fever the count is normal or increased, but when the temperature falls permanently the number of red cells falls suddenly, whether because the blood is diluted (see above, page 188) or by a real destruction. From this time on the cells are slowly regenerated; even at the fifteenth day Hayem found them considerably below normal.

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[1] Billings: Med. News, 1898, p. 301.

[2] Sobotka: Zeit. f. Heilk., 1893, p. 349.

[3] Courmont and Montagnard: Jour. de Phys. et Path. Gen., 1901, p. 63.

[4] Enriquez-Siccard: Soc. de Biol., December 1st, 1900.

In hemorrhagic cases the anæmia comes on more quickly, its degree depending on the amount of hemorrhage. In one patient, dying on the seventh day of the eruption, Hayem found but 2,000,000 red cells, in another at the same stage, 4,600,000.

Fibrin is not increased until the stage of suppuration is reached.

Leucocytes.

In Pick's report on 42 cases no leucocytosis is recorded until the appearance of vesicles.

Elaborate studies in the blood of smallpox have lately been published by Weil,[1] and by Courmont and Montagnard.[2] These studies are concerned especially with the leucocytes. In Weil's series of 36 cases the counts ranged between 6,000 and 10,000 in 6 cases, between 6,000 and 13,000 in 13 cases, exceeding 15,000 in 9 cases, exceeding 20,000 in 3 cases, 25,000 in 3 cases, 30,000 in 1 case, 35,000 in 1 case.

One case ranged from 3,000 to 6,000 during the whole course of the disease, except on the day of vesiculation (24,000), but this is very rare, and the leucocytes are usually increased from the beginning. The increase is usually most intense at the time of vesiculation, and from that time does not vary notably until after pustulation when it slowly declines until in convalescence a subnormal count is reached. In hemorrhagic cases the increase is usually less marked.

A sudden drop in the leucocytes count may occur in the fatal suppurating or hemorrhagic form. For example, in two fatal suppurating cases the leucocytes dropped from 24,000 and 18,000 to 6,200. In one hemorrhagic case on the dying day counts of 6,200, 6,000, and 4,400 were recorded. A sudden drop in the leucocytes is then a bad prognostic sign (from this opinion Courmont and Montagnard dissent).

Complications occurring in convalescence produce a second rise in the leucocytes.

Qualitative Changes.

The most significant fact in the blood of variola, according to the writers already quoted, is the increase in mononuclear cells. The percentage of polynuclear cells, instead of being increased as in most infectious diseases, is from the outset diminished (*i.e.*, 40 to 50 per cent), and may go as low as 14 to 20 per cent. Eosinophiles range from normal (1–3 per cent) at the beginning of the disease, downward. They are lowest just before desquamation. In convalescence they are often slightly increased.

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[1] Soc. de Biol., June 29th, 1900.

[2] Soc. de Biol., June 22d, 1900; July 6th, 1900.

Among the "mononuclear cells" the increase of which is held by Weil to be characteristic of the disease are:

(*a*) Small lymphocytes, 30–40 per cent.

(*b*) Large mononuclear, 4–10 per cent.

(*c*) Myelocytes, 2–10 per cent (even 25 per cent in hemorrhagic cases).

(*d*) Türck's "Reizungsformen," 2–10 per cent.

During suppuration and desiccation the mast cells are sometimes increased (5 per cent). The abnormal leucocytes—(*c*) and (*d*) above—are present from the very beginning of the disease and form a very characteristic part of the blood picture. They persist through pustulation and diminish only in convalescence. They are present in mild varioloids as well as in severe variola. Complication (pneumococcus or streptococcus septicæmia) do not materially modify the blood picture, unless they occur late in convalescence. In convalescence a polynuclear leucocytosis may result from suppurative complications.

Diagnostic Value.

In excluding scarlatina, measles, purpura, syphilis, erythema multiforme, the blood is conclusive. Varicella, on the other hand, produces changes in the blood which are precisely of the same type as those of variola, though less in degree.

VARICELLA (CHICKEN-POX).

The first observation of which I am aware is that reported by Engel.[1] In a child of five he found during the height of the pustular stage a moderate leucocytosis, with 67 per cent of neutrophiles (high for a young child), and no eosinophiles. Three days later, as the pustules were healing, the neutrophiles had sunk to 47 per cent (normal for that age) and the eosinophiles had risen to 16 per cent.

Nobécourt and Merklen (*Journ. de Phys. et Path. Gen.*, May, 1901) studied 15 cases and found in 10 of them a normal or subnormal leucocyte count and in 5 a very slight increase (highest = 14,500).

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[1] 15th Cong. für innere Med., 1897.

The polynuclear cells were increased in 6 and diminished in 7. The eosinophiles were always scanty; 5 of the patients showed myelocytes, one as high as 12.5 per cent. On the whole the blood seems not to be distinguishable from that of variola, although in most cases the total leucocyte count and the percentage of myelocytes are higher in variola.

Stengel and White (*loc. cit.*) found no leucocytosis in 2 cases, 12,800 in a third, and 19,200 in a fourth, which later developed pneumonia.

ACUTE ARTICULAR RHEUMATISM.

According to Hayem and Garrod[1] the blood constitutes, as in syphilis, a most valuable measure of the intensity of the sickness, which is parallel to the severity of the blood-changes rather than to the number of joints affected. The fever, the intensity of the lesions, and the state of the blood run parallel, in a general way, but the degree of anæmia is a more delicate index of the patient's condition than even the temperature chart (Garrod).

The Blood as a Whole.

Fibrin is greatly increased. In no other disease except in pneumonia is the network thicker or more rapid in formation. According to Maclagan, this is to be explained by an increase of tissue metamorphosis. Coagulation, on the other hand, is not quicker, but slower than usual.

Lactic acid is present in excess, but cannot be clinically estimated, nor is its excess peculiar to this disease.

The alkalinity of the blood had been reported diminished, but the technique is not considered reliable by the best observers.

Red Cells.—Hayem[2] and Osler[3] state that the poison of acute rheumatism is a powerful and rapid destroyer of red cells. In acute cases, according to Hayem, the red cells lose at least 1,000,000 of their number, and in cases which drag along and relapse the loss is from 1,500,000 to 2,000,000. When an attack is cut short by salicylate treatment the drain on the corpuscles is stopped. Türck's careful studies led him to the same conclusions. Red cells and hæmoglobin are always markedly diminished during the fever, the hæmoglobin especially, and after the attack a post-febrile anæmia of varying severity is always left.

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[1] British Medical Journal, May 28th, 1892.

[2] *Loc. cit.*, p. 917.

[3] "Practice of Medicine," 1895.

So far as my experience goes, this diminution does not seem to occur in all cases. Many of my cases had been sick some weeks before the time when the count was made, yet the counts are not very low. The average count of red cells in the whole group of cases is 4,300,000. The lowest counts were 2,528,000 with 45 per cent of hæmoglobin, 3,248,000 with 45 per cent of hæmoglobin, 3,456,000 with 50 per cent of hæmoglobin, 3,332,000 with 45 per cent of hæmoglobin, 3,468,000 with 36 per cent of hæmoglobin, 3,440,000 with 26 per cent of hæmoglobin, 3,608,000 with 40 per cent of hæmoglobin. Only 13 cases below 4,000,000 are recorded out of 113. McCrae[1] in 69 cases found the average to be 4,532,000 at the beginning of the disease and observed no diminution during the later course of most of the cases.

Qualitative Changes.—Maragliano's so-called degenerative changes in the red cells have been observed in this disease, but are not very marked. Türck found erythroblasts in about a quarter of his cases. Deformities in the red cells are usually slight.

Hæmoglobin.—As in all secondary anæmias the coloring matter is diminished more than the count. The average hæmoglobin percentage in this series is sixty-three, and the color index .73. McCrae (*loc. cit.*) states the average of hæmoglobin in 77 cases as 66 per cent, a figure practically identical with mine. The most marked change occurring in any case was a loss of 20 per cent in 12 days, the count of red cells being unchanged.

Leucocytes.—All observers agree that leucocytosis is the rule and that its degree is roughly parallel to the acuteness and severity of the attack (the individual's vigor of reaction is always a factor) and the amount of fever. Türck insists that complications (pneumonia, pericarditis, pleurisy) are present whenever the count rises over 20,000, and in this he is supported by Ewing. No such complications were discovered in many of the cases of Table XV. which exceed 20,000, but this table shows that in 80.5 per cent of 243 cases the leucocytosis was under 18,000. McCrae's average in 83 cases is 11,700; mine in 243 cases is 13,800. In 29 of his cases the count was 10,000 or less. The remaining 54 cases average 14,260, or 15,380 if the highest count is taken in each case. There were 17 cases with over 15,000 leucocytes, 4 with over 20,000, and 1 of 38,000. All cases complicated with pericarditis showed leucocytosis, but no constant connection between leucocytosis and endocarditis.

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[1] McCrae: f. Am. Med. Ass., January 24th, 1903

Rogers[1] noted leucocytosis (13,500 to 55,000) in 21 out of 23 cases. The following tables illustrate the variations of the leucocytes in a fairly typical way:

TABLE XV., A.—ACUTE ARTICULAR RHEUMATISM.

No.	Age.	Sex.	Duration.	Degree of inflammation.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	21	M.	5 weeks.	?	4,160,000	31,500	65	Knees and one ankle.
2	20	..	....	....	3,832,000	27,800	45	
3	59	F.	?	?	5,476,000	27,000	94	Patient pale.
4	20	..	?	?	4,392,000	26,000	50	
5	33	M.	2 weeks.	Red and hot.....	4,852,000	24,500	76	
6	Adult.	M.	?	?	4,216,000	21,000	56	
7	19	..	?	?	3,248,000	20,000	45	Died.
8	7	..	?	?	4,184,000	19,800	60	
9	23	..	?	?	3,792,000	19,600	45	Third day.
10	23	M.	4 weeks.	Tender and hot..	5,192,000	18,300	70	Temperature, 102°.
11	49	M.	?	?	4,800,000	17,700	..	Paronychia also.
12	46	..	....	....	4,934,000	17,400	55	
13	21	F.	?	Red and hot.....	3,944,000	17,000	45	Cheeks rosy.
14	37	.	....	....	5,224,000	16,300	58	
15	24	M.	2 days.	?	4,600,000	16,000	68	
16	32	..	....	....	4,832,000	15,800	57	
17	13	F.	1 day.	Red and hot.....	4,880,000	15,200	65	Temperature 102°.
18	12	M.	2 weeks.	Red and hot.....	4,400,000	15,000	56	
19	8	..	....	....	3,972,000	15,000	50	
20	20	..	....	....	4,872,000	15,000	58	
21	22	..	....	....	5,336,000	15,000	30	
22	19	M.	4 days.	Red and hot.....	4,760,000	14,500	75	Severe case.
23	41	..	....	....	4,397,000	14,500	40	Seventieth day.
24	9	F.	....	....	4,240,000	14,386	60	
25	47	M.	1 day.	Red and hot.....	4,750,000	14,000	75	
26	25	F.	3 days.	Tender and hot..	4,850,000	14,000	72	
27	18	F.	2 months	No redness or heat.	4,156,000	14,000	54	
28	19	M.	....	....	4,172,000	14,000	70	
29	19	M.	....	....	4,580,000	13,500	64	
30	29	..	....	....	4,720,000	13,200	65	
31	30	..	....	....	3,456,000	13,000	50	
32	32	..	....	....	5,440,000	12,800	55	
33	29	M.	....	....	4,320,000	12,750	68	
34	..	..	....	....	4,128,000	12,650	65	
35	37	F.	1 month.	Swollen and tender.	5,320,000	12,500	65	
36	30	F.	....	....	4,160,000	12,000		
37	47	M.	4 weeks.	Very slight......	4,288,000	12,000	65	
38	27	F.	3 days.	....	3,580,000	11,600	65	
39	17	M.	1 week.	....	4,600,000	11,500	70	
40	27	M.	10 days.	Hot and red.....	4,200,000	11,500	60	
41	28	..	....	....	4,888,000	11,300	50	
42	33	M.	4 weeks.	....	5,480,000	11,000	80	Hands alone involved.
43	42	..	....	....	3,882,000	10,400	45	
44	33	..	....	....	4,056,000	10,200	50	
45	26	..	....	....	4,728,000	9,400	40	
46	10	..	....	....	4,312,000	9,100	45	Mitral regurgitation.
47	20	F.	....	....	3,468,000	9,000	36	
48	36	..	....	....	4,716,000	8,000	50	
49	28	M.	3 weeks.	....	3,608,000	7,000	40	
50	Adult.	M	....	....	3,768,000	6,800		
51	29	M.	9 weeks.	Some joints hot..	4,104,000	5,500	58	Fourth relapse.
52	30	F.	....	....	3,440,000	4,700	26	Specific gravity, 1.040.
53	28	..	....	....	4,412,000	......	60	
54	14	..	....	....	4,240,000	......	46	
55	23	..	....	....	2,528,000	......	45	Twenty-second day.

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[1] Rogers: Lancet, September 6th, 1902.

TABLE XV., B.—ACUTE ARTICULAR RHEUMATISM WITH COMPLICATIONS.

No.	Age.	Reds cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	32	....	31,000	40	January 15th. Pericarditis,
			25,000	..	January 21st.
			24,000	..	January 26th.
			12,000	..	February 2nd.
2	8½	....	28,900	65	November 24th. Endocarditis.
			20,800	..	November 28th.
			17,500	..	November 30th.
			20,800	..	December 3rd.
			14,700	..	December 8th.
			7,700	..	December 11th.
3	18	....	27,000	90	Mitral and aortic insufficiency.
4	44	4,668,000	23,100	50	April 12th. Mitral insufficiency.
			37,600	..	April 14th.
			47,330	..	April 21st. Death.
5	13	.. ..	22,400	75	Mitral insufficiency.
6	22	....	21,600	80	February 25th. Mitral insufficiency.
			11,400	..	March 8th.
7	34	....	21,000	85	Mitral insufficiency.
8	43	....	20,600	75	April 30th. Mitral insufficiency.
			14,200	..	May 4th.
			8,200	80	May 14th.
9	25	....	20,350	60	June 1st. Pericarditis with effusion.
			16,600	..	June 3rd. Acute endocarditis.
			15,400	..	June 5th.
10	18	....	19,700	85	Mitral regurgitation.
11	33	....	19,400	70	Mitral stenosis.
12	24	....	19,300	80	December 7th. Pericarditis; endocarditis; mitral insufficiency and stenosis.
			15,300	..	December 10th.
			13,200	..	December 12th.
			14,300	..	December 19th.
			21,000	..	December 21st.
			30,300	..	December 23rd.
			22,100	..	December 24th.
			16,400	..	December 26th.
			14,100	..	December 29th.
			18,000	..	January 1st.
			18,600	..	January 5th.
			20,900	..	January 7th.
			18,000	..	January 9th.
			18,000	..	January 13th.
			12,000	..	January 15th.
				70	February 2nd.
13	23	....	18,800	74	Mitral insufficiency; aortic insufficiency. Flint.
14	25	....	18,400	70	July 24th. Mitral insufficiency.
			13,880	..	July 26th.
			11,500	..	July 30th.
15	24	....	18,000	85	Mitral insufficiency.
16	24	....	17,000	90	Mitral insufficiency.
17	22	....	16,500	80	Acute nephritis.
18	35	....	14,700	70	June 12th. Pneumonia.
			24,300	..	June 17th.
			13,400	..	June 21th.
			12,100	..	June 24th.
			0,450	..	June 2[illegible]th.
			19,600	..	June 29th.
19	58	....	14,260	58	Mitral insufficiency and stenosis; acute insufficiency.
20	26	....	14,200	90	Purpura.
21	40	....	13,500	85	Chronic rheumatism; cerebral hemorrhage.
22	18	....	13,300	85	Mitral insufficiency.
23	46	....	11,500	70	Chronic nephritis.
24	18	....	11,000	90	Mitral insufficiency.
25	30	....	10,000	90	Mitral insufficiency.
26	24	....	10,000	85	Aortic insufficiency.
27	30	....	9,800	75	Chronic interstitial nephritis.
28	16	....	8,400	85	Mitral disease.
29	26	....	8,400	75	Mitral insufficiency and stenosis.
30	23	3,892,000	8,400	23	Chlorosis.
31	34	3,228,000	8,000	40	Mitral insufficiency.
32	45	....	7,000	80	Mitral insufficiency.

ABLE XV., C.—ACUTE ARTICULAR RHEUMATISM.

White Cells.	Cases.
Between 6,000 and 8,000	11
“ 8,000 “ 10,000	30
“ 10,000 “ 12,000	39
“ 12,000 “ 14,000	35
“ 14,000 “ 16,000	45
“ 16,000 “ 18,000	36
“ 18,000 “ 20,000	18
“ 20,000 “ 22,000	8
“ 22,000 “ 24,000	6
“ 24,000 “ 26,000	7
“ 26,000 “ 28,000	2
“ 30,000 “ 32,000	3
“ 38,000 “ 40,000	3
	243

TABLE XV., D.—SUBACUTE ARTICULAR RHEUMATISM.

	ge.	Sex.	Red cell.	White cells.	Per cent hæmoglobin.	Remarks.
	31	..	....	39,000	80	September 5th.
				19,200	......	“ 7th.
				15,200	......	“ 9th.
				26,300	......	“ 11th.
				10,000	......	“ 18th.
				12,900	......	“ 22d.
2	42	..	....	34,000	85	April 24th.
				13,600	......	“ 26th.
3	26	..	....	26,800	80	“ 15th.
				15,200	......	“ 17th.
4	62	..	....	20,700	62	First day.
				13,700	......	Fourth day.
5	23	..	....	19,500	60	
6	33	..	....	18,200	85	
7	36	..	....	18,200		
				15,600	......	Sixth day.
8	32	..	....	17,500	70	
9	22	..	5,040,000	17,200	55	
10	23	..	....	16,000	45	
11	31	..	....	15,200	72	
12	25	M.	4,750,000	15,000	60	
13	68	..	....	14,900	55	
14	23	..	....	14,900	100	
15	13	..	4,430,000	14,500		
16	50	..	....	14,200	65	May 24th.
				6,800	......	May 28th; mitral regurgitation.
17	45	..	....	13,600		
18	30	F.	4,644,000	13,000	60	
19	15	..	3,820,000	12,000	50	
20	32	..	....	11,400	......	Temperature 100°.
21	28	F.	....	10,600	......	
22	25	..	....	10,500	......	

TABLE XV., D.—SUBACUTE ARTICULAR RHEUMATISM (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
23	33	..	....	10,500	......	Temperature 100.5°.
24	17	..	....	10,100	65	
25	53	..	....	9,900		
26	28	..	4,684,000	8,000	75	
27	?	..	....	7,800	60	
28	Adult.	M.	4,016,000	6,200		
29	Adult.	F.	4,188,000	5,750	73	

TABLE XV., E.—CHRONIC RHEUMATISM, CHIEFLY ARTICULAR.

No.	Age.	Sex.	Red cells.	White cells.	Per cent. hæmoglobin.	
1	40	..	....	13,500	85	
2	58	..	....	12,400	67	
3	29	..	... ...	12,400	85	
4	75	..	....	10,500	85	
5	55	..	....	10,200	80	
6	25	..	....	10,200	62	
7	20	M.	5,576,000	9,800	62	
8	33	..	... .	8,400	75	
9	19	F.	5,248,000	8,300	45	
10	24	..	....	8,300	67	
11	69	..	....	7,800	90	
12	78	F.	....	7,200	?	
13	46	..	....	7,000	85	
14	58	M.	4,744,000	6,500	60	
15	37	..	....	6,500	70	
16	32	..	....	6,400	?	
17	24	..	....	6,400	65	
18	30	F.	....	6,100	?	
			Average=	8,660		

TABLE XV., F.—SUBACUTE ARTICULAR RHEUMATISM.

White cells.	Cases.
Between 1,000 and 10,000	17
" 10,000 " 12,000	9
" 12,000 " 14,000	7
" 14,000 " 16,000	8
" 16,000 " 18,000	5
" 18,000 " 20,000	4
" 20,000 or more	3
Average = 11,000 +.	53

TABLE XV., E. "MUSCULAR RHEUMATISM."

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	46	M.	4,580,000	7,500	70	
2	52	..	4,370,000	4,000	55	
3	54	M.	4,380,000	7,500	75	
4	38	M.	?	6,600	?	
5	54	M.	3,820,000	14,000	58	During febrile attacks.
6	27	F.	?	6,000	?	Lumbago.
7	35	M.	?	5,700	?	"
			Average =	7,328 +		

The average leucocytosis in the acute cases is 13,800 in those mild and more chronic, so-called "*subacute,*" cases the leucocytes range lower, averaging 9,760; while in chronic rheumatism, whether articular or muscular (including lumbago), there is no increase at all (average = 7,450). In acute cases the leucocytosis subsides with the joints, rising again if relapse or complication occurs. The polynuclear cells are absolutely increased with an absolute diminution of the lymphocytes. The eosinophiles rarely disappear as in most infections. After the very earliest days (when they may be scanty or rarely absent) they are increased despite the fever and exudation. In convalescence they run even higher, 13.8 per cent (or 970 absolute) in one of Türck's cases. During the fever Türck noted myelocytes and stimulation forms as in other infections.

Blood plates are much increased during the fever.

In 32 cases of *arthritis deformans* treated at the Massachusetts General Hospital the blood was normal except for a slight deficiency of hæmoglobin in two cases.

Summary.

Slight secondary anæmia. Anæmia with leucocytosis, the degree of which is a measure of the severity of the infection.

Diagnostic Value.

The blood tells us little if anything that could not be learned in other ways. It does not differ at all from that of *septic arthritis* or from that of acute *gonorrhœal arthritis.*

The only cases that I remember in which a blood examination has been valuable are the following:

CASE I.—The patient had muscular pains, fever, and a history of a malarial attack some months earlier. The question to be decided by the blood examination was between malaria and "rheumatism." The leucocytes were 23,600 per cubic millimetre, which made it clear that the case was *neither* malaria nor "rheumatism," since the former never increases the leucocytes and the latter could give so high a count only in case genuine *articular* inflammation were present. The case turned out to be croupous pneumonia, which the high leucocyte count strongly suggested.

CASE II.—The patient presented symptoms and signs of acute polyarticular rheumatism with fever. The fever came down under salicylates, but soon rose again, and the man became wildly delirious. His delirium persisted after the salicylate was stopped. Several joints continued swollen and tender. The fever was very moderate, ranging between 99° and 101°. There were no rose spots and no enlarged spleen. The question arose as to whether it was a case of sepsis with localization in the joints, or whether it was a case of typhoid supervening on an arthritis of some kind. The blood count, which was repeated several times, always showed a perfectly normal blood except for a slight anæmia. The subsequent course of the case, during which he remained for nearly three weeks more or less delirious, made it clear to Dr. F. C. Shattuck, under whose care the patient was, that the diagnosis was typhoid.

Chronic rheumatism (muscular or articular) produces no constant blood changes appreciable by clinical methods (see Table XV., D and E).

ASIATIC CHOLERA.

In no other disease, so far as I am aware, has an *acid reaction* in the blood been reported. This is at the end of life. All observers agree that the alkalinity is at least greatly reduced.

Our knowledge of the corpuscles is best summed up in Biernacki's[1] study of 38, and Rogers[2] of 23 cases.

Red Cells.—In the *stadium algidum*, or stage of collapse, most of the symptoms are due to the great concentration of the blood from the loss of serious fluids in the stools. Hayem found the increase of red cells from this concentration to amount to from 1,000,000 to 1,500,000 per cubic millimetre.

Biernacki[1] found 7,662,500 in one case twenty-four hours after the beginning of the disease. The specific gravity may be as high as 1.071 or 1.072.

White Cells.—Leucocytosis is present, not merely as the result of concentration, but as a genuine increase to at least double the normal count. Biernacki[1] and Rogers[2] each found that cases with particularly high counts (20,000 to 60,000) were soon fatal, so that they consider a marked leucocytosis in the algid stage as a bad prognostic sign, although patients also die with low leucocyte counts in this period. Thus 11 out of 14 cases with counts over 20,000 died, while only 4 out of 9 cases with counts under 20,000 died (Rogers). Such a leucocytosis does not occur in ordinary diarrhœa or dysentery.

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[1] Biernacki: Deut. med. Woch., 1895, No. 48.

[2] Rogers: Lancet, September 6th, 1902.

Leucocytosis is present as early as twelve hours from the first symptom and lasts at least as late as the sixth day. In the stage of reaction it usually decreases. In one very mild case reported by Biernacki there was not only no increase, but leucopenia (4,375 per cubic millimetre), and Rogers noted counts of 2,000 and 4,000.

The differential count shows usually from eighty-two to ninety-five per cent of polynuclear cells and a corresponding diminution of the lymphocytes. Roger's figures seem to show that a large number of polynuclear cells (absolute and relative) and a small percentage (under 10 per cent) of lymphocytes means death in three-quarters of the cases, while more than one-half of the cases showing over 10 per cent of lymphocytes recovered. On the other hand an absolute and relative decrease of large mononuclear forms was associated with recovery in 4 cases out of 5, while of 18 cases with over 2,000 large mononuclear cells per cu. mm. 14 died. The eosinophiles are scanty. Sherrington[1] found the mast cells notably increased in some cases.

ERYSIPELAS.

Ehrlich, Halla, Pée, Reinert, Rieder, and von Limbeck agree that leucocytosis is usually present in well-marked cases. Von Limbeck finds the "leucocyte curve" to run roughly parallel with the temperature chart, sometimes beginning to fall a little before the latter. The counts rarely run very high, yet Reinert counted 39,627 in one case. Pée noted that the leucocyte count increases only while the process is spreading, and that the size of the count was a tolerably accurate measure of the severity of the case.

Rieder found in seven cases an average of only 15,000 per cubic millimetre despite very high temperatures. In one case the leucocyte count remained high after the temperature had fallen, but in the others it anticipated the temperatures. In one mild case he found no leucocytosis. Polymorphonuclear cells are greatly increased as in other forms of leucocytosis. Hayem noticed the same dependence of the leucocyte count upon the severity of the process.

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[1] Sherrington: Proc. Royal Soc., 1894, p. 189.

Chantemesse and Rey (*Presse Méd.*, 1899, vol. vi., p. 316) find that in most cases the degree of leucocytosis is parallel to the temperature curve, though the leucocytes may fall before the fever. In patients with average resisting power the highest counts accompany the highest temperature. When the area of disease extends the leucocytes generally rise. At the height of the fever the polynuclear cells are much increased at the expense of the other forms, while in defervescence these conditions are reversed.

From the third day to the end of the fever the polynuclear cells steadily diminish in favorable (adult) cases. In the aged the polynuclears are especially high, while in children the lymphocytes are increased, especially at the height of the process. Persistence and return of high polynuclear count means relapse, according to these writers.

TABLE XVI.—ERYSIPELAS.

Case.	Age.	White cells.	Remarks.
1	40	20,000	
2	28	14,400	First day.
		14,450	Second day.
		17,100	Third day.
		17,300	Fourth day; spreading.
		15,400	Temperature 105.°
3	25	16,600	
4	78	17,000	
5	29	14,000	
6	51	13,000	
7	38	12,400	
8	17	12,700	
9	32	10,300	
10	?	7,250	
11	21	6,200	

In eleven cases at the Massachusetts General Hospital I found leucocytosis in all but three, and these were very mild cases. As in most infections, the usual abnormal forms (stimulation forms and myelocytes) may be abundant at the climax of the process. Türck records five per cent of myelocytes (320 absolute).

When the disease occurred in "scrofulous" cases, Hayem found only 7,000–8,000 leucocytes per cubic millimetre, while in cases with very extensive process and high fever 12,000–20,000 were present. He found also a loss of 500,000–1,000,000 in the count of the red cells, according to the severity of the case. This showed itself particularly just before the fall of the temperature. I have seen no reference by other writers to the condition of the red cells in this affection.

TONSILLITIS (FOLLICULAR).

Halla[1], Pick,[2] and Pée[3] found leucocytosis as a rule in uncomplicated follicular tonsillitis; Rieder found it in a case complicated with acute nephritis.

The following table confirms these observations in the main, though in mild cases no leucocytosis was present.

TABLE XVII.—TONSILLITIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	19	..	....	41,000	90	Temperature 102.2 (acute).
2	20	..	....	36,000	85	Temperature 102.8 (acute).
3	2	..	....	34,400	....	
.	..	..	....	26,900	....	
..	..	..	....	26,300	....	
4	2	..	....	28,100	85	
5	7	..	....	28,000	..	
6	29	..	....	23,400	85	Acute follicular.
7	8	..	....	23,300	60	July 7th.
..	..	..	....	12,400	....	July 9th.
8	28	..	....	23,100	....	Dec. 24th. Follicular.
..	..	..	....	7,600	...	Dec. 26th.
9	19	..	....	22,600	80	Acute follicular. Nov. 1st.
..	..	..	....	14,500	....	Nov. 3d.
10	21	..	....	21,700	62	Acute follicular.
11	18	..	....	21,200	....	
12	22	..	....	21,000	90	Feb. 2d. Acute.
..	..	..	....	18,000	....	Feb. 8th.
13	22	F.	4,368,000	19,200	35	
14	22	..	....	18,500	...	
15	27	..	....	18,200	100	
16	26	..	....	18,100	....	
17	21	F.	....	18,000	....	
18	24	..	....	18,000	....	Acute follicular.
19	27	M.	....	18,000	....	
20	20	..	....	17,500	75	
21	37	..	....	17,400	75	
22	12	..	....	17,300	....	Streptococcus.
23	28	..	....	17,000	95	
24	23	..	....	16,800	....	
25	21	F.	....	16,800	....	Acute follicular.
26	25	F.	....	16,200	....	
27	30	F.	4,750,000	16,000	80	Temperature 101.
28	28	..	....	16,000	80	
29	24	..	....	16,000	....	

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[1] Zeitschrift f. Heilk., 1883, p. 198.

[2] Prag. Med. Woch., 1890, p. 308.

[3] Pée: Inaug.-Dissert., Berlin, 1890, p. 8.

TABLE XVII.—TONSILLITIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
30	27	M.	....	15,500	67	Six days ; slight.
31	32	..	....	15,000	....	
32	24	..	....	14,800	100	Acute follicular.
33	16	..	....	14,400	80	
34	43	..	....	14,200	90	August 1st.
..	..	..	....	14,600	....	August 5th.
..	..	..	....	14,400	....	August 8th.
..	..	..	....	16,800	....	August 8th.
35	Adult.	F.	4,860,000	14,000	....	Follicular.
36	17	..	....	14,000	80	Acute.
37	30	M.	4,730,000	13,500	76	Convalescent.
38	24	F.	5,000,000	13,500	68	Follicular.
39	Adult.	M.	....	135,000	....	
40	24	..	....	13,300	....	
41	36	..	....	13,200	....	
42	24	..	....	13,200	90	Follicular.
43	.	M.	4,952,000	12,250	94	
44	28	..	....	12,000	....	Acute.
45	24	F.	5,816,000	11,900	65	Streptococcus; slight articular rheumatism.
46	..	M.	5,000,000	11,800	90	Follicular
47	19	F.	4,552,000	11,600	65	Temperature 104.3. Aortic Regurgitation.
48	18	M.	5,150,000	11,500	83	Chronic recurrent, out in two days.
49	26	..	....	11,000		
50	24	..	....	11,000	65	
51	23	..	....	10,900	68	Follicular.
52	22	..	....	10,500	90	
53	18	..	....	10,000	80	
54	22	F.	5,016,000	9,600	....	
55	27	..	....	9,200	80	August 12th.
..	..	..	....	8,200	....	August 14th.
56	24	..	....	9,100	65	Temperature 102. Follicular.
57	16	..	....	9,000	70	Temperature 100.4. Follicular.
58	38	..	....	8,800	70	January 15th. Follicular.
59	23	F.	....	7,925	52	Follicular; slight; temperature 99° next day.
60	34	..	....	7,700	....	Bronchitis.
61	45	F.	....	6,800	....	
62	19	..	....	6,500	90	
63	Adult.	..	4,200,000	5,800	60	Follicular.
64	27	..	....	5,800	85	Follicular.

At the close of the attack a slight eosinophilis has been noted by several observers.

The blood examination has no diagnostic value so far as I am aware. It is worth knowing that a simple tonsillitis can cause leucocytosis, to the end that if such is discovered on blood examination we need not suppose that some other process is present to account for the increase.

GRIPPE.

"Grippe" is a term very loosely used to designate any infection of relatively short course, especially if catarrhal symptoms are present. Seldom is the diagnosis established by satisfactory bacteriological evidence. In all probability, therefore, many of the cases included in the table below are not true "influenza."

The references to the hæmatology of the disease in literature are very scanty. Orion (*Archiv. d. Méd. milit.*, 1890, p. 280) found fibrin increased during the early days of the disease. Rieder (*Münch. med. Woch.*, 1892, xxxix.) found no leucocytosis in grippe and but little in the "catarrhal pneumonia" following it (Türck).

Blum (*Wien. klin. Woch.*, April 13, 1899), found normal or subnormal counts, the latter especially in the "abdominal" type of the disease. Gerber (*ibidem*, 1900, Nos. 25-27) and Stengel report figures much like mine, *i.e.*, rarely over 15,000 per cu. mm.

The following table shows that the leucocytes are normal in about two-thirds of the cases. One hundred and seven of the three hundred and nine cases showed leucocytosis, but in several of these some complication was very possibly present. Only 34, or 11 per cent, showed over 15,000 leucocytes. The absence of leucocytosis is of importance in excluding *pneumonia* and *local inflammatory* conditions. The leucocyte count does not help us to distinguish the disease from *typhoid*. In this decision the serum reaction is our mainstay (see page 529). From malaria it may be distinguished by the absence of malarial organisms. In one case, after an operation for traumatic epilepsy, the temperature rose to 104°, with a chill, and the question of meningitis was considered. The absence of leucocytosis excluded the meningitis, and the attack turned out to be grippe, which was just then very prevalent.

TABLE XVIII.—GRIPPE.

White Cells.

Between 2,000 and 3,000 = 3 cases.
" 3,000 " 4,000 = 8 "
" 4,000 " 5,000 = 15 "
" 5,000 " 6,000 = 22 "

TABLE XVIII.—GRIPPE (*Continued*).

White Cells.

Between	6,000	and	7,000	= 40	cases.
"	7,000	"	8,000	= 25	"
"	8,000	"	9,000	= 28	"
"	9,000	"	10,000	= 33	"
"	10,000	"	11,000	= 27	"
"	11,000	"	12,000	= 24	"
"	12,000	"	14,000	= 33	"
"	14,000	"	15,000	= 17	"
"	15,000	"	16,000	= 10	"
"	16,000	"	17,000	= 7	"
"	17,000	"	19,000	= 5	"
"	19,000	"	20,000	= 6	"
"	20,000	"	21,000	= 2	"
	21,000	+		4	"
			Total	= 309	"

Red Cells.

Between	3,000,000	and	4,000,000	= 8	cases.
"	4,000,000	"	5,000,000	= 10	"
"	5,000,000	"	6,000,000	= 15	"
				28	"

SEPTICÆMIA.

Puerperal septicæmia, infected wounds, septic arthritis, septic endocarditis, general infections with pyogenic bacteria, "pyæmia," are all identical so far as their effects on the blood are concerned, and will be considered together under the general head of Septicæmia.

Bacteriology of the Blood.

Cocci can be demonstrated in cultures from the blood of septicæmia more frequently than in any other class of infections. Rosenbach[1] in 1884 found streptococci and staphylococci in sepsis.

Garré[2] in 1885 found the last-named coccus in a case of osteomyelitis. In 1890 v. Eiselsberg[3] found staphylococci in ten cases of septic wounds and one case of osteomyelitis, and streptococci and staphylococci together in five more patients whose wounds had become septic.

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[1] "Microorganismen b. d. Wundinfectionskrankheiten," etc. Wiesbaden, 1884.

[2] Fortsch. d. Med., 1885, No. 6.

[3] Wien. klin. Woch., 1890, No. 30.

Czerniewsky,[1] Stern, and Hirschler[2] found the same organisms in puerperal fever, the former observer in five cases.

Brunner,[3] Hoff,[4] and Blum[5] found pyogenic staphylococci in pyæmia and sepsis, and Saenger,[6] Roux and Lannois,[7] Cantu[8] and Bommers[9] had equal success, each in a single case.

Canon[10] and Sittman[11] investigated large numbers of cases with many positive results, and Grawitz[12] and Petruschky[13] and Cohn[14] were successful in finding pyogenic cocci in the blood of cases of ulcerative endocarditis as well as in other septic infections. Herschlaff[15] found them in erysipelas, acute tuberculosis, perforated typhoid ulcer, etc. Kühnau,[16] on the other hand, was unable to find anything in the blood of twenty-three severe pyæmic cases, and was successful in only one out of twelve cases of ulcerative endocarditis.

Taking the results of all these investigators together with those of White,[17] Krauss,[18] James and Tuttle,[19] Brieger[20] and Neumann,[21] we get a total of 316 cases, with 107 positive results, or 33 per cent. I agree with Da Costa that these figures give too favorable an impression as to the value of blood culture in sepsis. Still Grawitz insists that if we are not content with a single trial in negative cases, the *majority of cases* show the presence of pyogenic organisms, and that in obscure septic cases the diagnosis may be greatly facilitated by such an examination. Negative results are of course very far from excluding septicæmia, but positive ones are sometimes of great value if proper precautions are taken in the technique of the examination. In the diagnosis of malignant endocarditis, often a most difficult one, Grawitz thinks blood cultures are especially important and likely to prove positive when the disease is present (see Diseases of the Heart, p. 346).

[1] Archiv f. Gynäkol., 1888, No. 33.

[2] Wien. med. Presse, 1888, No. 28.

[3] Wien. klin. Woch., 1891, No. 20.

[4] Dissert, Strassburg, 1890.

[5] Münch. med. Woch., 1893, No. 16.

[6] Deut. med. Woch., 1889, No. 8.

[7] Revue de Méd., No. 12.

[8] Rif. Med., 1892, No. 96.

[9] Deut. med. Woch., 1893, No. 16.

[10] Deut. Zeit. f. Chirrug., 1893, p. 571.

[11] Deut. Arch. f. klin. Med., 1894, p.573.

[12] Charité-Annalen, 1804, vol. x.

[13] Zeit. f. Hygiene, 1894, pp. 59 and 413.

[14] Deut. med. Woch., 1897, No. 9.

[15] Sem. Méd., 1897, p. 105.

[16] Deut. med. Woch., 1897, No. 25.

[17] White: Jour. of Exp. Med. 1889, vol. iv., p. 425.

[18] Krauss: Zeit. für Heilk., 1896, vol. xvii., p. 117.

[19] James and Tuttle: Report of Presbyterian Hosp., 1898, p. 46.

[20] Brieger: Charité-Annalen, 1888, p. 198.

[21] Neumann: Berl. klin. Woch., 1888, vol. xxv., p. 143.

Almost all observers agree that the finding of pyogenic cocci (except the staphylococcus albus) in the blood makes the prognosis almost surely fatal. The *toxicity* of the blood is doubled.

Red Cells.—All observers agree that very marked anæmia is present in severe cases. Red marrow post mortem I have seen in two instances. Roscher's[1] investigations tend to show that the diminution in red cells in septicæmia is greater than in any other infective disease, and appears in a shorter time. He found such a diminution present no longer than a few hours from the beginning of the illness. He finds the amount of anæmia proportional to the severity of the case, and (reckoning by means of the estimated solid residue) concludes that whenever the blood has lost one-quarter of its substance or more, death follows. He considers, therefore, that help as to prognosis is given us by the blood examination in septicæmia.

The serum becomes very watery, partaking of the general atrophy of the blood tissue. In a case of intensely acute puerperal sepsis, with profuse uterine bleeding, Grawitz found the red cells reduced to 300,000 (!) although the patient had been sick less than twenty-four hours. The case seems almost incredible, but is reported in great detail in the author's recent text-book, to which reference has so frequently been made. He accounts for it by the combination of hæmolysis and dilution.

In eleven cases of puerperal sepsis seen at the Massachusetts General Hospital in recent years the red cells averaged 3,500,000, which is very low, considering the shortness of the illness in most cases. (The influence of hemorrhage during parturition must of course be taken into account.)

In most of the septic wounds which I have seen the counts have not been low. But in one case of septicæmia from a suppurating fibroid of the uterus the red cells numbered only 1,800,000. Ewing reports a septic endometritis with 1,600,000 red cells. In a case of puerperal sepsis of only a few days' duration, in a woman not previously anæmic, Hayem[2] recently reports the following figures:

December 3d—	Red cells	1,450,000
	White cells	7,500
	Hæmoglobin	20 per cent.
December 6th—	Red cells	2,578,000
	White cells	8,000
	Hæmoglobin	40 per cent.

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[1] Inaug. Dissert., Berlin, 1894.

[2] La Méd. Moderne, January 13th, 1897.

r 24th—Red cells 4,231,000
White cells.......... ... 7,200
Hæmoglobin .... 65 per cent.
(Recovery.)

h cases are the best examples we have of an *acute anæmia* rhage excepted).

hæmoglobin is usually diminished about as much as are the es.

eated red cells are very often seen; whether or not they gnostic value cannot yet be stated. In differential diagno- presence helps us to exclude typhoid and miliary tubercu- in which diseases they rarely are found.

TABLE XIX.—PUERPERAL SEPTICÆMIA.

	ge.	Sex.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
		F.	....	77,500	..	Autopsy.
		F.	2,300,000	26,000		
		F.	3,900,000	23,900	68	Two days before delivery.
				21,000	..	Day of delivery.
				9,500	..	One day after delivery.
				15,500	..	Five days after delivery; breasts caked.
				15,000	..	Ten days after delivery.
				11,800	..	Twenty-six days after delivery.
4	28	F.	3,784,000	22,000	55	Miscarriage five days before; septic; curetted.
				13,600	..	Three days later, temperature falling.
				8,300	..	Seven days later, temperature normal.
				15,800	..	Fourteen days later, temperature up; curetted again.
				14,900	..	Fifteen days later, temperature falling.
				15,000	..	Sixteen days later, temperature falling.
				9,500	..	Thirty-two days later, temperature falling.
5	25	F.	....	20,800	55	
6	34	F.	....	15,900	..	September 2d, 1897.
				35,600	..	September 9th, chills.
				33,000	..	September 13th.
				35,600		September 16th. Recovered.
7	25	F.	2,936,000	20,000	50	April 1st, 1894.
				21,090	.	April 3d, 1894.
8	32	F.	4,904,000	19,300	..	Curetted.
				9,300	..	One week later, well.
9	24	F.	3,556,000	18,400		
10	..	F.	....	Marked increase	..	Polymorphonuclear cells, 94%; lymphocytes, 6%.

TABLE XIX.—PUERPERAL SEPTICÆMIA (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
11	26	F.	5,368,000	5,600	..	Died.
12	24	..	3,428,000	33,500	45	With general peritonitis.
				28,800	..	Secondary operation.
13	19	..	3,536,000	9,600	..	July 18th. Pelvic cellulitis. Diff. count 500 cells (chlorosis). Polynuclear, 73%; lymphocytes (s.), 22; lymphocytes (l.), 4; eosinophiles, 1%. Reds slight irregularity in size and shape. No nucleated reds seen.
				6,800	..	July 29th.
14	23	..	4,400,000	14,500	45	May 2d. With toxic nephritis.
				13,400	..	May 9th.
				7,400	..	May 14th.
				17,500	..	May 24th.
				12,200	..	May 28th.
				9,300	..	June 3d.
15	26	..	4,056,000	12,400	30	June 8th. Secondary anæmia. Polynuclear, 86.6%; lymphocytes (s.), 9.4%; lymphocytes (l.), 3%; eosinophiles, .8%; myelocytes, .2%. Reds stain palely in centres, moderate poikilocytosis and irregularity in size. Normoblasts, 1.
				14,800	..	June 14th.
				18,400	..	June 28th.
16	27	..	....	12,200	..	December 5th.
				8,200	..	December 9th.
				11,400	..	December 11th, died. P., 140–170; T., 103°–105°; R., 35–60.
17	40		....	9,200	..	T. 104°. Recovered.
18	28	F.	....	23,400	75	Jan. 22d.
				13,600		" 23d.
				15,200	..	" 24th.
				14,900	..	" 25th.
				8,400	..	" 27th.
				16,200	..	" 29th.

TABLE XX., A.—SEPTIC WOUNDS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	37	F.	5,880,000	48,400	....	Sloughing breast; bedsore.
2	28	M.	7,600,000	25,400	....	Septic wound of foot.
3	31	F.	5,680,000	15,300	....	Sloughing breast after cancer operation.
			5,840,000	23,200	....	One month later; wound clean.
4	27	M.	4,450,000	10,500	....	Septic hand.
5	..	M.	5,600,000	8,800	....	Septic finger.

TABLE XX., B.—SEPTICÆMIA WITH ARTHRITIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	8	M.	....	25,000	..	Pus in elbow joint ; no injury.
				43,000	..	Two days after operation, vent not free ; opened further.
				24,000	..	Seven days after operation.
				20,700	..	Eight days after operation.
				6,700	..	Sixteen days after, well.
2	21	..	....	23,800	..	T. 101°.
3	34	M.	....	19,000	65	Gonorrhœal pus in knee.
4	59	M.	4,520,000	18,500	..	Pus in shoulder joint ; no trauma.
5	28	..	....	18,200	..	T. 99°.
6	22	..	....	17,500	72	Gonorrhœa and syphilis.
7	55	..	....	17,500	.	Gonorrhœal.
8	?	..	....	17,100	..	Gonorrhœal.
9	28	..	....	16,500	..	Gonorrhœal.
10	42	..	....	14,100	50	Gonorrhœal.
11	22	..	....	13,800	..	Gonorrhœal ankle.
12	16	..	....	13,300	52	Gonorrhœal.
13	32	..	3,864,000	12,500	..	T. 99°. Gonorrhœal.
14	32	..	....	12,200	..	T. 102°. Gonorrhœal.
15	33	..	....	11,900	..	Gonorrhœal.
16	32	..	....	9,700	..	T. 101°. Gonorrhœal.
17	21	..	....	9,400	..	Gonorrhœal.
18	28	..	....	9,100	..	Gonorrhœal.
19	28	..	....	9,000	..	Gonorrhœal.
20	39	M.	....	8,940	..	Ankle gonorrhœal. Cultures negative.
21	?	..	....	8,800	76	Gonorrhœal.
22	32	..	....	6,200	..	T. 101°. Gonorrhœal.
23	21	..	....	6,200	..	Gonorrhœal.

TABLE XX., C.—GENERAL SEPTICÆMIA.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	36	..	....	62,900	90	Temp. 104°. Pulse, 92. Apex 220. Cardiac dilatation. Death.
2	Adult.	M.	5,248,000	41,400		
3	"	F.	1,800,000	46,000	....	Suppurating fibroid. Streptococcus.
4	22	F.	3,776,000	25,800	53	A fatal case, yet *no fever!* Streptococcus.
5	65	..	....	25,200	65	June 30th.
				24,900	..	June 30th.
				20,400	..	July 1st.
				28,600	..	July 3d.
				31,700	..	July 4th.

TABLE XX., C.—GENERAL SEPTICÆMIA (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
				24,800	..	July 5th.
				23,500	..	July 6th.
				24,000	..	July 8th.
						June 30th. Differential count, 400 cells.
						Polynuclear, 86.
						Small lymphocytes, 5.5.
						Large lymphocytes, 8.
						Eosinophiles, 0.5.
6	44	..	....	20,700	..	Cholangitis.
				30,700	..	Pus in eye and throat. Streptococcus.
7	43	..	....	12,100	..	Cause?
8	20	..	....	27,000	..	Septic leg, pus burrowing.
9	11	..	....	10,800	..	December 15th.
				13,000	..	December 17th.
				18,600	.	December 19th.
				19,400	..	December 20th.
				13,200	..	December 21st.
				12,200	..	December 23d.
				12,400	..	December 23d.
				10,400	..	December 28th.
				11,000	..	January 5th.
				22,000	..	January 15th.
				34,000	..	January 19th. Autopsy.
10	33	..	....	24,000	75	April 24th.
				19,400	..	April 26th.
				18,000	..	May 1st.
				19,600	..	May 3d.
				43,200	..	May 11th. T. 104⅘°. No autopsy.
11	55	..	....	10,100	..	Pneumococci in blood. Autopsy.
12	33	..	4,160,000	22,000	45	Multiple septic embolism. Sugar in urine.
				16,000	..	Tenth day.
				22,000	..	Seventeenth day. Autopsy.
13	38	..	....	19,800	..	First day.
				29,100	..	Third day.
				27,200	..	Fourth day.
				25,200	..	Sixth day.

Deformities in the shape and size of the corpuscles are not usually marked except in the severest cases. Ewing has noted a reduction in the diameter of the cells in anæmic cases.

Hæmoglobinæmia with reddish staining of the serum is often noticeable in the dried and stained cover-glass specimen when the plasma is deeply stained.

Leucocytes.—Considerable controversy has taken place as to the changes in the white cells in puerperal septicæmia; some observers finding leucocytosis, while others find none.

The results of experimental infections referred to above (see page 102) and the parallelism of the leucocyte changes in pneumonia, peritonitis, and diphtheria fully explain these apparent divergences, which perfectly exemplify the rules stated on page 97.

Leucocytosis occurs only when the struggle between the patient and his disease is intense, and whichever is victorious. When either side wins without any difficulty, *i.e.*, in the mildest and in the severest cases, leucocytosis is nearly or entirely absent; indeed, leucopenia may be found (as for instance in a case of septic endometritis reported by v. Limbeck—only 3,000 leucocytes). Von Limbeck and Krebs[1] found no leucocytosis in cases of puerperal septicæmia, but these were all fatal cases or very mild ones. Rieder, on the other hand, and the great majority of other observers (Sadler,[2] Roscher,[3] Kanthak,[4] Grawitz, etc.) find leucocytosis. This means that in most cases observed by these writers the infection was of moderate severity. Ewing's experience leads him to the conclusion that while the rule that suppuration produces leucocytosis is almost invariable, it must be remembered that leucocytosis may promptly disappear when exudation ceases, and that suppuration involving mucous surfaces may induce very slight leucocytosis.

Only 14 of the 56 cases in Tables XIX. and XX. showed no leucocytosis. One was very mild, the other proved fatal on the day of the count. The leucocytosis is of the ordinary polynuclear type with disappearance of eosinophiles and diminution of lymphocytes. Myelocytes and "stimulation forms" are usually present in small numbers. Iodophilia is always marked, and may be of value in the diagnosis of cases with leucopenia. The reappearance of the eosinophiles seems to me to have some favorable prognostic significance.

[1] Krebs: Dissert., Berlin, 1893.

[2] Sadler: *Loc. cit.*

[3] Roscher: Dissert., Berlin, 1894.

[4] Kanthak: Brit. Med. Journal, June, 1892.

Summary.

1. Rapid development of severe anæmia.
2. Leucocytosis marked, except in very mild or very severe cases.
3. Blood cultures may contain pyogenic cocci.

Diagnostic Value.

The advantage of a positive bacteriological examination is obvious. Of the value of the blood count in distinguishing septic from non-septic wounds and estimating the degree of sepsis and the importance or needlessness of operative interference a great deal has been written within the last three years. The question will be thoroughly discussed in connection with appendicitis (see page 249).

Local Suppurative Process.

The effects of abscess upon the blood are, I suppose, due to septicæmia. Nevertheless septicæmia *with* abscess formation differs enough from septicæmia *without* abscess formation, both clinically and hæmatologically, to make a separate description convenient.

The most easily studied variety of abscess is that connected with appendicitis, inasmuch as the frequency of operations in such cases gives us opportunity to verify what we suppose to be indicated by the blood count and see how far our suppositions are true.

At the Massachusetts General Hospital, most patients with other varieties of abscess go straight to the surgeon and their blood is not examined, but many cases of appendicitis come first to the medical wards, and hence we have records of nearly one thousand cases whose blood has been examined.

I shall therefore begin the description of the blood in abscess by an account of appendicitis, which may probably be considered a typical case of abscess formation.

APPENDICITIS.

In the following table I present a small group of the Massachusetts Hospital cases, which represents fairly well the conditions found in average cases:

TABLE XXI.—APPENDICITIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	42	M.	5,400,000	58,000	....	Question of typhoid; pus found at operation.
2	40	M.	6,800,000	43,000	....	Chronic case; 95 per cent. of polynuclear leucocytes.
3	30	F.	....	39,900		
4	..	....	5,184,000	36,700		
5	..	....	4,800,000	36,000		
6	50	M.	4,990,000	35,000		
7	..	....	6,000,000	34,000	....	Three days after operation.
8	..	....	6,500,000	34,000	....	Seven " " "
9	?	M.	5,072,000	28,000		
10	..	....	....	24,900	....	Second attack; operation at 11 P.M. November 5th, count at 5:30.
				16,850	... ...	Serous peritonitis found. November 6th, 5 P.M.
				15,600	....	November 7th, 3 P.M.
				10,700	....	" 8th, 4 "
				15,100	....	Temperature still up. November 9th, 5 P.M.
				14,600	....	November 10th, 5:30 P.M.
				11,800	....	" 11th, 8:30 "
				17,850	....	" 12th, 8:30 "
				18,900	....	" 13th, 8 A.M.
				13,100	....	" 13th, 8:30 P.M.
						Recovery complete ten days later.
11	..	....	, ...	24,000	....	24° September 1st; operation, free turbid fluid without adhesions.
				12,500	....	September 10th.
				19,500	....	" 12th; pocket of pus found.
12	23	M.	5,200,000	24,000		
13	..	....	5,144,000	23,000	88	January 14th.
				16,100	....	" 15th: before operation, ℥v. + pus.
14	..	M.	....	22,500	....	Not operated; entrance.
				13,000	....	Second day.
				9,500	....	Third "
15	..	M.	....	22,300	....	12:20 operated; belly full of pus.
				9,500	....	8:30 moribund; blood dark and hard to get.
16	35	F.	....	22,000	....	July 6th.
				19,400	....	" 8th.
				14,900	....	" 10th, T. 104°; recovery.
17	..	M.	....	21,900	....	Appendicitis eight to nine days; operation; post-cæcal abscess.
18	..	....	....	21,700	....	November 5th, first operation.
				21,400	....	" 10th.
				16,000	....	" 13th.
				24,400	....	" 15th.
				20,200	....	" 16th.
				47,700	....	" 19th, second operation (pus pocket).
				16,700	....	" 20th.
				13,000	....	" 21st.
				10,700	....	" 22d.
				30,300	......	" 26th, third operation (pus pocket).
				20,900	....	" 27th.
				17,700	....	" 28th.
				25,100	....	" 29th.
				28,100	....	" 30th.
				20,400	....	December 1st.
				15,400	....	" 2d.
				25,000	....	" 3d.
				11,900	....	" 4th.
				15,600	....	" 5th.
				21,900	....	" 6th.
				19,000	....	" 7th.
				11,900	....	" 8th.
				12,800	....	" 9th.
				11,700	....	" 10th.
				12,300	....	" 11th.
				15,600	....	" 12th.
				13,400	....	" 13th.
				14,700	....	" 21st.
				16,500	....	" 25th.
				11,300	....	" 26th
19	31	M.	... .	20,540	....	October 5th.

TABLE XXI.—APPENDICITIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
19	31	M.	....	33,000	....	October 6th.
				14,640	....	" 8th.
				9,200	....	" 9th; moved bowels.
				21,000	....	12th; tender still and tense.
				24,900	....	99° to 100° temperature.
				13,700	....	Normal: still sore.
20	..	M.	....	....	....	Appendicitis twenty-four hours; resistant belly.
				20,100	....	October 23d.
				14,000	....	" 24th, 9 A.M.
				12,400	....	" 24th, 4 P.M.
				13,250	....	" 24th, 11 P.M.; not operated.
				8,750	....	" 25th, 8 A.M.; liquids every two hours.
				9,600	....	" 25th, 3 P.M.
21	24	F.	....	20,000	....	May 24th.
				19,000	....	" 25th.
22	..	....	....	20,000	....	June 5th; temperature, 101.4°; pain and vomiting.
				9,000	....	June 7th; no pain.
				10,000	....	" 8th; no pain; temperature, 100.6°; discharged.
23	..	....	4,800,000	20,000	....	Operated; pus.
24	..	....	5,564,000	20,000		
25	..	....	4,670,000	19,750	....	January 13th.
			5,296,000	15,000	....	" 15th.
26	20	F.	....	19,600	....	" 29th.
			4,680,000	12,000	....	February 1st.
			4,688,000	8,933	....	" 5th; after operation.
27	..	....	....	19,500	....	No operation.
28	58	M.	5,120,000	19,000	....	Purulent peritonitis.
29	20	M.	5,680,000	18,930		
30	14	M.	....	18,000		
31	..	....	....	17,500	....	Accident case; operation; pint of pus under pressure.
32	25	M.	....	16,250	....	Fifth day. November 7th.
				17,450	....	November 8th.
				12,000	....	" 11th; not operated; well on 17th.
33	25	M.	....	16,200		
34	..	....	....	16,200	....	Eighth day; operation; large abscess cavity.
35	40	F.	....	16,051	....	Operated.
36	..	....	....	16,000	....	Entrance.
				8,000	....	Same evening; no operation
				7,500	....	Next day.
				6,800	....	" "
37	..	....	6,160,000	16,000	....	General peritonitis,
38	..	....	....	16,000	....	November 12th, noon.
				8,000	....	" 12th, 8:30 P.M.
				7,500	....	" 13th, 8 A.M.; not operated.
				6,600	....	" 13th, 8 P.M.
39	..	....	3,300,000	16,000		
40	17	M.	4,380,000	15,600	66	March 25th, 9 P.M.; vomiting, pain, tenderness.
				19,500	....	" 27th; comfortable, no vomiting; signs more localized.
				22,900	....	" 28th; slight tenderness only.
				35,300	....	" 29th; bowels move well; no symptoms.
				32,800	....	" 30th; operation; large amount of pus.
41	27	M.	4,330,000	15,523		
42	23	M.	5,910,000	15,330		
43	22	M.	....	14,800	....	20th; general peritonitis.
				10,000	....	21st; " "
44	..	....	....	14,700	....	Five days; third attack; operation; free turbid fluid, no perforation; prompt recovery.
45	36	F.	4,250,000	14,700	70	27th, 8 P.M.
				13,150	....	28th; symptoms less; no operation.
46	23	F.	....	14,400	....	February 23d, } ℥ij. foul pus.
				10,300	....	" 24th, }
47	..	....	4,950,000	14,000	....	Catarrhal.
48	..	....	....	13,400	....	3 P.M., November 9th; appendicitis twenty-four hours.
				11,200	....	5 P.M., November 10th; temperature, 98.8°.
49	..	....	5,000,000	13,000		
50	..	....	....	13,000	....	Visible tumor. March 27th.
				17,000	....	" " April 26th, operated; pus.
51	..	....	4,626,000	12,000		

TABLE XXI.—APPENDICITIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
52	..	M.	....	12,000	....	Appendicitis cake. August 3d, operation; gangrenous appendix with adhesions.
				16,900	....	August 6th, fæcal fistula.
53	..	M.	....	11,900	....	No symptoms except pain for twenty-four hours; not operated.
54	51	M.	....	11,800	....	Very slight tenderness; no resistance or dulness. July 6th.
				19,900	....	Temperature up; tenderness and resistance. July 7th, operation; pus found.
				11,700	58	December 28th, 4 P.M.
55	..	M.	4,860,000	17,600	....	" 30th, 10 A.M.
				16,670	....	" 31st, 11 "
				11,950	....	January 1st, 9 P.M.
				10,800	....	" 5th.
				10,875	....	July 27th; nine days pain and vomiting.
56	22	F.	4,664,000	21,000	....	July 28th; more pain, tenderness and vomiting; operation showed pus.
				10 700	....	November 7th, appendicitis six days.
57	..	M.	....	9,000	....	Operation; abscess with considerable pus; gangrenous perforated appendix with concretion in it.
				10,500	....	Not operated till later.
58	12	F.	3,690,000	10,400	....	February 6th, 12 M.; slight pain and tenderness.
59	46	M.	....	9,800	....	" 7th, 3 P.M.; temperature dropping.
				10,400	....	Catarrhal.
60	..	...	5,600,000	10,500	....	"
61	..	M.	....	10,140	....	One week, fourth attack; no cake, no acute symptoms; operation; no pus.
				10,040	....	Sixth day, operation; abscess, ℥i. pus.
62	..	M.	....	9,000	....	Operated; no pus; catarrhal.
63	..	M.	....	8,400	....	December 1st.
64	24	F.	....	10,000	....	" 6th.
				7,200	....	" 15th.
				7,600	....	" 16th.
				7,700	....	No pus.
65	..	....	5,106,000	7,600		
66	..	....	5,600,000	7,600	....	No operation.
67	..	....	6,500,000	7,600	....	No pus.
68	..	..	6,500,000	7,050	....	Catarrhal appendix; five days in hospital.
69	31	M.	....	7,000	85	Catarrhal appendix.
70	47	M.	6,000,000	6,600	....	" chronic; nearly well; operation; no pus.
71	56	M.	....	6,000	....	" or very slight.
72	22	F.	4,320,000			

From the seventy-two cases of the adjoining table, together with about six hundred other counts not here recorded, the following conclusions are to be drawn:

1. Red cells: no changes except in chronic cases with long-standing abscess.

2. Coagulation often slow, but fibrin always increased in suppurating cases.

3. As in most infections, the mildest and the severest cases show no leucocytosis. *Six cases with general purulent peritonitis showed no leucocytosis,* its absence being confirmed by repeated examinations. The total absence of leucocytosis in a case not obviously mild is a very bad prognostic sign as in pneumonia and diphtheria.

4. Catarrhal appendicitis is rarely accompanied by leucocytosis (only once in this series—14,000). In Da Costa's 38 cases of "catarrhal and interstitial" appendicitis there were but four with counts above 15,000.

5. *An increasing leucocytosis means a spreading process and may be the only evidence of the fact.* In Case 40 of this series, the patient entered with vomiting, localized pain and tenderness. The leucocytosis was 15,600. Three days later he was comfortable, had no vomiting and very little tenderness, and in all respects seemed to be improving, yet the white cells had risen to 22,900. Operation was postponed owing to the lack of all unfavorable symptoms *except the blood count.* Next day the bowels were moving well and the patient *had no fever and no bad symptoms of any kind,* but his leucocytes had risen to 35,300. On the following morning the surgeon was finally persuaded to operate and found a large amount of pus. Four times this series of events has fallen under my observation.

A steadily increasing leucocytosis is always a bad sign and should never be disregarded even when (as in these cases) other bad symptoms are absent. It is of far more significance than a larger count which does not increase.

6. The size of the leucocytosis is of comparatively little significance. A low count (8,000–11,000) means one of three things:

(*a*) A mild case.
(*b*) A very severe case.
(*c*) An abscess thoroughly walled off.

After the abscess has ceased to spread and has become well walled off, the leucocyte count remains stationary or decreases. If it bursts into the general peritoneal cavity the count may rise sharply or it may fall to normal or subnormal, its movement depending on the degree of resistance which the system offers.

7. In the majority of cases the pus is neither completely walled off nor free in the belly, and such cases are accompanied by a moderate and fluctuating leucocytosis, which rises and falls according to a variety of conditions which cannot be accurately interpreted.

It usually increases in the first three or four days of the illness, and then becomes stationary or declines if the case is taking a favorable course (*i.e.*, if the pus is being absorbed or walled off), while it continues to increase when the case is going on from bad to worse.

Case 20 illustrates the course of the leucocytes in a favorable case not operated on; the leucocytes fell gradually but steadily from hour to hour so that in two days the count came down from 20,100 to 8,750, the tumor and tenderness simultaneously disappeared, and the patient was well in a few days more. Case 38 dropped in eight hours from 16,000 to 8,000 and quickly recovered. In Case 19, the leucocytosis fell in three days from 33,000 to 9,200, but rose again when the bowels were moved by enema, and took some days to reach normal again. Evidently the peristalsis injured the abscess wall so that the process began to spread again and had to be walled off afresh.

8. When a leucocytosis of 18,000–25,000 is maintained for a number of days it usually means a large abscess pretty well walled off.

9. The majority of cases as seen at the Massachusetts General Hospital on the second, third, and fourth days of the illness showed leucocytosis of 15,000–24,000, thirty-three of the present series falling within these figures. Counts larger than this have always been proved to mean a large amount of pus, a general peritonitis, or a complication such as pylephlebitis or hepatic abscess. Of the cases below 15,000 (fifteen in all) twelve did not come to operation, or if operated showed no pus. This statement excludes the four cases of general purulent peritonitis without leucocytosis mentioned above.

10. Case 18 illustrates several points. After the first operation the leucocyte count did not fall so rapidly as usual, and the cause of this soon turned out to be a pus pocket, after the evacuation of which the count fell in twenty-four hours from 47,700 to 16,700, only to rise again for another accumulation of the same kind.

After this last (third) operation the case progressed slowly but favorably, and yet the leucocyte count remained more or less above normal for a month. The wound was healthy, freely discharging, and had healed satisfactorily at the time of the last count reported.

Bloodgood[1] has studied a considerable group of cases with much care and his results deserve our attention. He properly lays great stress upon the element of *time* in the interpretation of leucocyte counts. He divides his cases primarily into the *acute* and the *chronic*, and then makes a second set of distinctions among the acute cases, which will concern us later.

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[1] Bloodgood: Prog. Medicine, December, 1901.

I. The 29 *chronic cases* in his series (all operated upon) include those admitted at the end of an attack, or between attacks, and found at operation to be unassociated with pus. Twenty-four of these had counts below 12,000, while the other five ranged between 12,000 and 15,000. The latter were in cases admitted at the end of an attack and still presenting slight symptoms.

II. (*a*) *Acute Diffuse Appendicitis without Pus* ("catarrhal").

In 22 cases (all operated on) there was one count of 22,000 (twenty hours from the first symptom), rapidly falling to 11,000 within twenty-four hours, and two counts of 17,000, falling within forty-eight hours to normal. The other cases showed lower counts.

(*b*) *Gangrenous Appendicitis* (10 cases, no pus).

In cases seen early in the attack a rapid rise of the leucocyte count can be observed to 20,000 or more.

(*c*) *Acute Appendicitis with Pus Distending the Organ.*

The counts in four cases were practically like those in gangrenous appendicitis.

(*d*) *Appendicitis with Abscess.*

In 14 cases of Bloodgood's series (26 per cent) the leucocyte count was normal (6,000–12,000). In 11 of the 14, the history and the other symptoms pointed to a chronic, well-encapsulated abscess. In 3 there were acute local symptoms, and 2 of these were extremely ill—presumably unable to react.

In 9 cases—subacute or chronic with palpable tumor—the counts ranged between 12,000 and 15,000.

In 33 cases (63 per cent) the leucocytes numbered 15,000 to 60,000—the great majority over 18,000. All were above this figure if seen within the first forty-eight hours.

(*e*) *Appendicitis with General Peritonitis.*

The counts may be high or low. Four of Bloodgood's cases showed respectively 11,000, 11,000, 13,000, and 14,000 (all fatal). These were all cases of at least three days' duration, and as in cases observed within the first forty-eight hours, he has often (as I have) found high counts, he concludes that "in the early hours of peritonitis there is a rapid rise in the leucocytes, which, however, soon falls."

In view of all these facts, Bloodgood considers that: "Within the first forty-eight hours a leucocytosis of 18,000 should be considered an indication for operation," especially if we have recorded *a rising* leucocyte count. With a count below 18,000 *and falling* the patient is recovering from the attack.

Between the third and seventh day a leucocytosis of 18,000 or more is usually an indication for immediate operation, but in some cases the local signs may incline us to postpone operation.

The above agrees essentially with the opinion of Longridge,[1] of Kühn,[2] of Coste,[3] of Locke,[4] and of Joy and Wright.[5]

The latter observers lay especial emphasis on the *good prognostic significance* of a *decreasing leucocytosis.* In such cases, unless the falling count is accompanied by unmistakable signs of a generally bad condition (which is rarely the case), operation may be postponed, while a *high stationary or increasing count indicates a progressively serious case* which demands immediate intervention. This is entirely in agreement with my own experience.

Curschmann,[6] Kuttner,[7] Dützmann,[8] Blassberg,[9] and Weiss[10] express similar views, Kuttner especially insisting upon the need of making at least two counts a day and controlling them with the iodine reaction (see below). If carried out with these precautions Kuttner considers the count of leucocytes a most valuable aid in distinguishing post-operative aseptic fever from pus-pocketing. Curschmann believes that a single count of 25,000 or more should make us very suspicious of the presence of pus, though, like all other recent observers, he deprecates reliance on single isolated counts and urges leucocyte charts. Blassberg believes that leucocytosis is less marked in peripheral than in abdominal suppurations.

From these quotations it appears that our German colleagues are at last waking up to the importance of blood counts in suspected deep abscess, and are going through for the first time experiences familiar to American physicians since 1893. Indeed, there are indications that some German surgeons are falling into the error so common here ten years ago—the error of supposing that leucocytosis always means pus. Against this mistake Grawitz warns his countrymen in the latest edition of his excellent text-book. Deaver[11] in this country has uttered similar and on the whole very valuable warnings against the "tendency to replace the bedside by the laboratory as the point from which to make the diagnosis." *When such a choice must be made* sensible men will generally agree with Deaver that the bedside is the point of vantage. But as Da Costa and others have pointed out, we need rarely make this most unfortunate division between the different methods of physical diagnosis. The microscope should be a "laboratory" instrument no more than the thermometer.

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[1] Longridge: Brit. Med. Journal, November 8th, 1902.

[2] Kühn: Münch. med. Woch., December 9th and 16th, 1902.

[3] Coste: *Ibidem*, December 9th, 1902.

[4] Locke (see p. 255).

[5] Joy and Wright: Medical News, April 5th, 1902.

[6] Curschmann: 31st German Surgical Congress, April, 1902.

[7] Kuttner: *Ibidem.*

[8] Dützmann: *Ibidem.*

[9] Blassberg: Wien. klin. Woch., November 20th, 1902

[10] Weiss: *Ibidem*, January 15th, 1903.

[11] Deaver: Transactions of Am. Surg. Assn., 1901, p. 115.

The matter cannot be better summed up, I think, than in the words of Da Costa: "The surgeon who attempts to use the blood count in appendicitis as a definite pathognomonic sign will soon run afoul of diagnostic disasters, but he who regards it only as a symptom invariably to be correlated with equally, if not more important, clinical manifestations, cannot fail to find this method of inquiry of signal value in routine clinical surgery."

I am likewise in hearty agreement with another statement of Da Costa's: "The behavior of the leucocytes throws a much clearer light upon the *progress* of the disease, both in operative and non-operative cases, than it does upon the *initial diagnosis*, which should be determined chiefly by other clinicial methods." But to interpret aright the variations of the leucocytes after operation, we need to be familiar with those changes in the blood due to the operation itself, and to the anæsthetic which made it possible. Accordingly, I shall next discuss:

I. The Effects of General Narcosis on the Blood; and

II. Post-Operative Changes in the Blood.

I. THE BLOOD CHANGES PRODUCED BY GENERAL NARCOSIS.

The earlier literature is well summarized by Da Costa and Kalteyer.[1] Their own studies in fifty cases lead them to the following conclusions:

1. Following anæsthesia there is generally a polycythæmia, rarely an oligocythæmia. The polycythæmia is most marked immediately after the termination of the anæsthetic stage, probably due to a concentration of the blood from previous purgation and recent vomiting.

2. Hæmoglobin is invariably reduced absolutely, although the amount of ether used and the duration of anæsthesia probably influence the blood change to a moderate extent.

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[1] Da Costa and Kalteyer: Annals of Surgery, September, 1901.

3. The amount of blood lost by operative hemorrhage seems to have little effect upon these changes.

4. Owing to the hæmolysis following anæsthesia, the writers believe that no operation can be safely done when the hæmoglobin is below fifty per cent.

Fish[1] has previously reached similar conclusions, while Mikulicz puts the percentage at 30. Bloodgood[2] details a case in which the red cells fell from 3,076,000 before operation to 2,000,000 twenty-four hours later, while the hæmoglobin fell from 54 per cent to 30 per cent, despite the fact that there was practically no loss of blood at the operation.

Despite all this important evidence, which goes to show the narcosis may be dangerous in anæmic patients, we must not forget that it may be even more dangerous to postpone operation. Hence it may be the surgeon's duty to operate under local anæsthesia or to face the danger of general narcosis as the lesser of two evils.

The Leucocyte Count During and After Narcosis.

The studies of Da Costa and Kalteyer (*loc. cit.*) and of Cabot, Blake, and Hubbard[3] have proved that the effect of etherization on the leucocytes is practically nil. They were unable to confirm the results of Chadburne.[4]

II. Post-Operative Changes in the Blood.

In the studies of Cabot, Blake, and Hubbard counts were made after full anæsthesia and again at the close of the operation in 36 cases. In 11 of these (30 per cent) there was a distinct leucocytosis varying from 19,000 to 27,000, which appeared to be due rather to the nature and extent of the operation than to the anæsthetic. King's[5] studies indicate that an increase of from 5,000 to 10,000 over the count before operation is a very common phenomenon within the first forty-eight hours following operation and is of no significance *provided it is not sustained.* The maximum is reached within twelve hours after operation.

White[6] found an average of nearly 21,000 per cubic millimetre after laparotomy with an absolute (and usually relative) increase of polynuclear cells and absence of eosinophiles.

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[1] Fish: Annals of Surg., 1899, vol. xxx., p. 79.

[2] Bloodgood: Prog. Med., December, 1900.

[3] Cabot, Blake, and Hubbard: Annals of Surg., 1901, p. 361.

[4] Chadburne: Phil. Med. Jour., February 18th, 1899.

[5] King: American Jour. Med. Sciences, 1902, vol. cxxiv., p. 450.

[6] White: Univ. Med. Mag., May 13th, 1901.

The degree of leucocytosis seemed to depend upon the severity of the operation. The highest counts were found about five hours after operation. From this time the number of leucocytes gradually diminished, reaching normal, on the average, in about five days.

If complications occur, the leucocyte count remains elevated, or is slower in falling. Frazier and Holloway[1] who studied forty cases and did not confine themselves to laparotomies, found that three and one-half days was the average duration of post-operative leucocytosis in uncomplicated cases. White found that in cases sewed up tight the leucocytes returned to normal more rapidly than in those drained. In the latter cases the slight infection along the drainage tube probably accounted for the fact that the post-operative leucocytosis usually lasted more than five days. My own observations tally very closely with the above and I shall not repeat them in detail.

Iodophilia.

The studies of E. A. Locke[2] in sixty-one cases of appendicitis are so interesting that I have inserted his tables entire. The leucocyte count and the iodine reaction were taken immediately before operation and their indications carefully compared with the pathological conditions found at operation.

TABLE XXII.—INTERVAL APPENDICITIS.

No.	Intracellular.	Extracellular.	Whites.	Remarks.
1	Absent.	Slightly increased.	9,000	Temp. 98.8°. No inflammation. Adhesions.
2	Absent.	Slightly increased.	11,000	Numerous adhesions. No inflammation.
3	Absent.	Normal	12,000	Few adhesions. No inflammation.
4	Absent.	Normal	7,000	Temp. 98.8°. Many adhesions.
5	Absent.	Slightly increased.	8,000	Temp. 99°. Many adhesions. No inflammation.
6	Absent.	Slightly increased.	10,500	Old adhesions and moderate inflammation.
7	Absent.	Slightly increased.	12,000	Appendix thickened and adherent.
8	Absent.	Normal	12,000	Chronic inflammation.

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[1] Frazier and Holloway: Univ. of Penn. Med. Bull., December 1901.

[2] Locke: Journal of Medical Research, January, 1902 (literature here abstracted), and Boston Medical and Surgical Journal, September 11th, 1902.

TABLE XXIII.—ACUTE APPENDICITIS WITHOUT GENERAL PERITONITIS OR LOCAL ABSCESS.

No.	Intracellular.	Extracellular.	Whites.	Duration.	Remarks.
1	Faint	Increased.	22,000	3 days.	Temp. 101.1°.
2	Faint	Increased.	24,000	....	Temp. 101.6°. Appendix much inflamed.
3	Faint	Normal...	14,000	......	Small, red appendix, with adhesions.
4	Faint	Normal...	20,000	....	Appendix moderately inflamed.
5	Slight coloration	Increased.	15,000	8 hours.	Temp. 100°. Appendix considerably inflamed.

TABLE XXIV.—APPENDICITIS WITH LOCAL ABSCESS, BUT WITHOUT GENERAL PERITONITIS.

No.	Intracellular.	Extracellular.	Whites.	Duration.	Remarks.
1	Faint	Increased.	14,000	4 days.	Few drops pus walled off.
2	Fair	Normal ..	17,000	....	Gangrenous appendix. Small abscess.
3	Fair	Increased.	15,000	....	Temp. 101°. Big abscess.
4	Fair	Normal ..	27,000	....	Temp. 101.6°. Few drops pus.
5	Fair..........	Increased.	....	....	Perforated appendix. Small amount of pus.
6	Good	Increased.	20,000	4 days.	Temp. 104°. Appendix gangrenous. Small abscess.
7	Good	Normal ..	14,000	....	About one ounce pus.
8	Good	Increased.	18,000	... .	Small abscess well walled off.
9	Good	Increased.	....	....	Gangrenous appendix. Small abscess.
10	Good	Increased.	24,000	4 days.	Temp. 102°. Pus burrowing beneath the mesentery.
11	Marked	Increased.	7,400	....	Enormous abscess. Death in few hours.
12	Marked	Increased.	20,000	....	Perforated, local peritonitis.
13	Marked	Normal ..	16,000	6 days.	Small pocket of pus. Temp. 102.9°.
14	Marked	Increased.	10,000	24 hours	Temp. 105°. Small abscess.
15	Marked	Increased.	21,000	3 weeks	Temp. 101°. Large abscess.
16	Marked	Increased.	36,000	... .	Small amount of pus not walled off.
17	Marked	Normal ..	30,000	....	Gangrenous appendix. Little free pus.
18	Marked	Normal ..	25,000	3 weeks	Small abscess walled off.
19	Marked	Increased.	8,000	3 days.	Temp. 102.5°. Pus not walled off.
20	Marked	Increased.	20,000	6 days.	Temp. 99°. Pus partially walled off.

TABLE XXV.—APPENDICITIS WITH GENERAL PERITONITIS.

No.	Intracellular.	Extracellular.	Whites.	Remarks.
1	Very marked.	Much increased.	40,000	Much free pus.
2	Very marked.	....	24,000	Perforated appendix and mild general peritonitis.
3	Marked	Much increased.	20,000	Temp. 101°. Streptococcus infection.
4	Marked	Normal	28,000	Considerable free pus.
5	Marked	Increased ..	27,000	Perforated appendix. Much free pus.
6	Marked	Increased ..	13,400	Perforated appendix. Little free pus.
7	Marked	Increased ..	14,000	Temp. 105.5°. Traumatic origin.
8	Marked	Normal ...	16,000	General infection of peritoneum. No pus.
9	Marked	Increased ..	4,800	Abdomen full of pus.
10	Marked	Greatly increased.	8,000	Abdomen full of pus.
11	Marked	Greatly increased.	13,000	Abdomen full of pus.
12	Moderate	Normal	....	Appendix abscess. Not walled off.
13	Good	Normal	19,000 15,000	Perforated appendix. Early peritonitis.
14	Good.........	Increased ..	52,000	No free pus.
15	Good.........	Increased ..	33,000	Temp. 103.6°. Extensive inflammation.
16	Good....	Increased ..	25,000	Temp. 99.7° No pus.
17	Good.........	Normal	18,000	Temp. 103.°
18	Good.........	.. ..	12,000	Typhoid perforation. No pus. Six hours' duration.
19	Fair	Increased ..	17,000	Temp. 102.8°. Free fluid. Culture sterile.
20	Fair.........	Increased ..	30,000	Bullet wound of abdomen. At autopsy some general inflammation, but no pus.
21	Faint	....	12,000	Temp. 98°, nine hours after perforation of gastric ulcer. Mild inflammation. No pus.

In general the intensity of the intracellular reaction appears to indicate the severity and duration of the process on the appendix and the amount of septic absorption from the focus. When the amount of pus is small and thoroughly encapsuled (as in Table XXIV., Case I.) the reaction may be faint. But the point of greatest interest is the *occurrence of a marked iodine reaction without leucocytosis in some of the most virulent cases.* (See Table XXIV., cases 11, 14, and 19, and Table XXV., cases 9 and 10.) Here the indications of the iodine reaction act as a most valuable control and correction upon those of the leucocyte count.

With the free drainage of pus, the brown granulation in the leucocytes rapidly diminishes, and is usually gone within forty-eight hours. Persistence of the reaction indicates incomplete drainage. The iodine reaction, like the leucocyte reaction, means usually septicæmia, but not always pus. It is present in cases of grave anæmia, and in a variety of toxic and infectious conditions (malaria, uræmia, grave anæmia, carbon monoxide poisoning, etc.), some of which produce leucocytosis, while others do not. Its value consists in the fact that it adds another to our list of clinical indications of the presence of toxæmia—such indications as pyrexia, tachycardia, albumosuria, and leucocytosis. None of these is present in every case and any of them may be present when toxæmia is absent. Hence the addition of an independent indicator like iodophilia to our list strengthens our diagnostic resources considerably.

Occasionally we have infectious or suppurative processes without pyrexia or tachycardia. Rarely we have infectious or suppurative processes without pyrexia, tachycardia, or leucocytosis. Never (so far) have infectious or suppurative processes occurred without pyrexia, tachycardia, leucocytosis, or *iodophilia.*

The diagnostic value of a negative reaction is therefore great, for as Locke says:

"Septic conditions of all kinds, including septicæmia, abscesses and local sepsis, except in the earliest stages, appendicitis accompanied by abscess formation or peritonitis, general peritonitis, empyema, pneumonia, pyonephrosis, salpingitis with severe inflammation or abscess formation, tonsillitis, gonorrheal arthritis and hernia, or acute intestinal obstruction where the bowel has become gangrenous, have invariably given a positive iodophilia, and by its absence all these cases can be ruled out in diagnosis. In other words, no septic condition of any severity can be present without a positive reaction."

On the other hand, he has failed to get a positive reaction in extra-uterine pregnancy, in dry and serous pleurisy (sixteen cases), in uncomplicated tuberculosis, in bronchitis, and in articular rheumatism (twelve cases).

The further indications of the iodine reaction will be considered in the sections on the different diseases investigated.

Differential Diagnosis.

1. The presence of a marked leucocytosis excludes simple *colic with or without constipation.*

2. *Post-operative malaria*, which may break out in patients who are aware of no previous attacks or who have had none for months, produces fever and chill like those due to pus-pocketing peritonitis, pylephlebitis, or other post-operative complications. The discovery of the malarial parasite and the absence of any marked leucocytosis serve to identify malaria, while in the other affections leucocytosis is high and persistent.

3. Treves[1] has reported several cases in which it was hard to decide whether the diagnosis was *typhoid* or appendicitis. A blood examination would probably have decided the matter, as it has in three cases in the writer's experience. Most cases of appendicitis of any severity show leucocytosis; typhoid almost never does if uncomplicated. Curtis[2] reports a case of typhoid with a tumor and tenderness in the right iliac region which closely simulated appendicitis, but turned out to be a floating kidney. The blood count would have decided the matter.

4. Between *appendicitis and pus tube* the blood gives no help, as both affect it alike.

5. *Ovarian or pelvic neuralgia* (uncomplicated) never causes leucocytosis and may be excluded by its presence. The same is true of floating kidney, which has been sometimes confounded with appendicitis.

6. *Gall-stone colic*, and *renal colic* if uncomplicated by inflammatory disturbance, cause no leucocytosis, and can therefore be distinguished from appendicitis in most cases. If cholangitis, cholecystitis, pyelitis, or severe cystitis complicate the colic, the examination of the blood will be no help to us.

7. *Impaction of fæces* in the cæcum will not cause any leucocytosis and may be excluded when such is present. The count may be of use, it seems to me, in deciding us whether an enema ought to be given. It is sometimes desirable to give an enema in cases simulating appendicitis, to help clear up the diagnosis; but some physicians are afraid to do so for fear of causing a walled-off abscess

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[1] Medico-Chirurgical Transactions, 1888, lxxi., p. 165.

[2] Twentieth Century Practice of Medicine, vol. viii., p. 461.

to break into the general peritoneal cavity. In such cases, if no leucocytosis were present, we might go ahead with a clearer conscience.

Mr. B—— entered the Massachusetts General Hospital, September 20th, 1893, with a diagnosis of appendicitis. For twenty days he had been having pain and tenderness in the region of the appendix, pain being controlled by morphine. The bowels had been loose, he said. There were dulness, tenderness, and a distinct tumor in the region of the appendix, with slight pyrexia. The blood count showed only 8,000 leucocytes. He was given a compound cathartic pill, had a large movement of the bowels, and all symptoms and signs disappeared.

8. *Extra-uterine pregnancy* and pelvic hæmatocele may cause leucocytosis like appendicitis, but *do not increase fibrin* unless peritonitis is present, and are likely to *show a marked diminution in red corpuscles* if the hemorrhage is severe. The red cells are normal in appendicitis except in chronic cases with abscess.

9. *Floating kidney* has been already mentioned in Curtis' case, in which in combination with typhoid it closely resembled appendicitis. Even without the presence of typhoid, the same difficulty of diagnosis may arise between appendix and floating kidney. The presence of leucocytosis could not be accounted for by the latter.

One of the next most common forms of abscess seen in medical wards is pyosalpinx, which I shall call by the English name of "pus tube." As this produces the same effect on the blood as appendicitis or any other abscess I shall not repeat the general considerations just discussed.

PUS TUBE, PELVIC ABSCESS, AND PELVIC PERITONITIS.

Almost all that has been said of appendicitis applies equally well to these conditions.

TABLE XXVI., A.—PUS TUBE AND PELVIC ABSCESS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	42	F.	....	46,000	80	January 2d. General peritonitis; double pus tube; **Death.**
				44,000	....	January 5th.
				45,000	....	January 7th.
2	36	F.	....	43,000	....	Double pus tube; too weak to operate. **December 15th.**
				31,000	....	December 22d.
				45,900	....	December 29th; abscess burst per vaginam.

TABLE XXVI., A.—PUS TUBE AND PELVIC ABSCESS—*Continued.*

No.	Age.	Sex.	Red cells.	White cells.	Per cent haemoglobin.	Remarks.
				20,200	....	January 4th, abscess opened in groin.
				15,200	....	January 8th.
				12,200	....	January 11th.
3	..	F.	5,400,000	34,200	....	Pelvic abscess.
4	38	F.	....	34,200	....	Pus tube. June 18th.
				34,600	....	June 19th.
				35,000	....	June 20th.
				40,000	....	June 27th, fever and vomiting just before catamenia.
				17,300	....	July 1st, temperature normal.
				11,500	....	July 8th, mass decreasing.
				12,000	....	July 14th, slight thickening still.
5	10	F.	....	33,500	65	Acute localized peritonitis.
6	34	F.	4,202,000	35,500	60	Pus tube; septic arthritis; jaundice.
7	..	F.	4,880,000	30,000	....	Pus tube.
8	23	F.	....	29,200	....	Double pus tube.
9	29	F.	4,544,000	28,800	....	General purulent peritonitis.
10	20	F.	....	27,300	....	Pus tubes.
11	26	F.	3,800,000	27,000	65	Double pus tube. November 17th.
				25,000	....	November 19th, operated.
12	25	F.	....	27,000	65	August 22d, pelvic abscess.
				20,000	....	August 24th.
13	43	F.	5,210,000	26,600	....	Pus tubes.
14	25	F.	....	25,400	85	Pelvic abscess.
15	28	F.	5,120,000	24,400	....	Pus tube.
16	..	F.	....	24,400	....	Pus tube four weeks' duration.
17	24	F.	5,376,000	24,000	....	Pus tube.
18	21	F.	....	23,600	85	November 11th. Pus tube.
				12,000	....	November 13th.
19	..	F.	3,760,000	23,000	....	Pelvic abscess (fetid pus).
20	27	F.	....	22,600	85	February 8th. Pelvic abscess.
				17,500	....	February 10th.
				10,000	....	February 11th.
				12,900	....	February 15th.
				16,900	....	February 17th.
				13,200	....	February 19th.
				18,000	....	February 21st.
				19,400	....	February 23d.
				20,400	....	February 24th.
21	45	F.	....	22,000	....	Pus tube.
22	..	F.	5,200,000	22,000	....	Pus tube.
23	..	F.	5,200,000	22,000	....	Pus tube; operation; pus found.
24	35	F.	3,704,000	21,100	65	Pus tube operated.
25	19	F.	....	20,200	....	May 1st.
				23,800	....	May 11th, mass the same; pus tube.
26	26	F.	5,021,000	20,000	....	Pus tube.
27	..	F.	4,400,000	19,800	....	Pus tube.
28	21	F.	....	19,000	....	Pus tube. Temperature 99°. April 26th.
				21,100	....	No fever. May 2d.
				16,000	....	May 4th.
				18,600	....	May 9th.
				19,600	....	No fever.
				21,600	....	May 18th, flow of pus from os started by manipulation.
				18,200		
				16,300	....	Outdoors.
29	54	F.	3;940,000	19,000	60	Pus tube and ovaritis; operation; pelvis full of foul pus; recovery, after hysterectomy.
30	25	F.	3,860,000	18,800	....	Pus tubes.
31	?	F.	4,592,000	18,800	....	Pus tube.
32	21	F.	....	18,600	68	July 31st, pelvic abscess.
				16,000	....	August 1st.
				13,000	....	August 6th.
				18,000	....	August 11th.
33	18	F.	3,840,000	18,500	55	Pus tube; three hours after food.
34	32	F.	5,776,000	18,000	....	Pus tubes.
35	28	F.	5,000,000	18,000	....	Pus tube.
36	30	F.	3,410,000	18,000	....	Pus tube, etc.
37	21	F.	5,088,000	16,400	....	Pus tube, syphilis. October 7th.
			5,184,000	18,000	....	October 12th.
38	22	F.	4,300,000	16,000	80	Pus ear.
39	..	F.	3,800,000	16,000	....	Pus tube

TABLE XXVII., A.—PUS TUBE AND PELVIC ABSCESS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
40	35	F.	....	15,600	....	Pus tube. May 8th.
				18,200	....	May 18th, transferred.
41	36	F.	4,656,000	15,600	60	Pus tube; large amount of pus found.
42	21	F.	....	15,500	90	December 31st, salpingitis.
				4,500	....	January 2d.
43	50	F.	....	15,400	80	May 6th, pus tube.
				21,600	....	May 9th.
44	19	F.	....	15,300	....	Pelvic peritonitis.
45	36	F.	3,696,000	14,975	48	Pus tube. July 21st, chills and delirium.
				12,600	....	July 23d.
						July 25th; operated.
46	20	F.	4,310,000	14,800	30	Pus tube; chlorosis.
47	26	F.	....	14,700	60	Pus tube.
48	21	F.	....	14,700	65	January 17th, pus tube.
				11,200	....	January 18th
				9,000	....	January 19th.
				9,000	....	January 20th.
49	38	F.	3,008,000	13,853	22	Pus tube.
50	25	F.	....	13,500	75	Pus tube.
51	22	F.	....	13,000	95	Jan. 1st, pus tube.
				10,000	....	Jan. 2d.
				26,800	....	Jan. 8th.
				15,000	....	Jan. 10th.
				11,000	....	Jan. 14th.
				6,000	....	Jan. 19th.
				14,800	....	Jan. 25th.
				15,000	....	Jan. 30th.
52	..	F.	4,700,000	12,500	70	Pus tube (double); operated.
53	35	F.	....	12,200	....	Pus tube; slight.
54	21	F.	....	12,200	....	Pus tube. June 2d
				12,300	....	June 10th.
55	19	F.	3,910,000	12,000	....	Pus tube.
56	36	F.	....	12,000	90	Pus tube.
57	..	F.	4,756,000	11,850	63	Pus tube. January 5th and 6th.
				13,750		
58	18	F.	....	11,300	75	Pus tube.
59	33	F.	4,240,000	11,000	55	Pus tube. Not operated; very slight.
60	18	F.	....	10,800	70	Pus tube.
61	47	F.	....	10,600	....	Chronic salpingitis. June 21st.
				11,000	....	June 25th, better.
				11,500	....	June 29th.
62	21	F.	3,800,000	10,400	64	Pelvic peritonitis.
63	44	F.	....	10,200	70	June 3d, pus tube.
				14,130	....	June 24th.
64	..	F.	7,000,000	10,000	....	Pelvic abscess (?).
65	38	F.	4,125,000	10,000	60	Pelvic abscess. August 28th.
				17,000	....	September 3d, temperature up.
				13,400	....	September 6th, normal temperature.
66	24	F.	....	9,900	....	Pus tube.
67	19	F.	....	9,800	64	November 16th, Pus tube.
				20,900	....	November 27th.
				14,000	....	November 30th
68	19	F.	....	9,200	85	Pus tube.
69	24	F.	....	9,000	....	Salpingitis, 9 A.M.; Temp. 99.4°.
				9,200	....	4:15 P.M.: five days in hospital.
70	19	F.	....	8,900	80	Pus tube.
71	23	F.	....	8,200	80	Pus tube.
72	21	F.	....	8,200	80	Pus tube.
73	21	F.	....	8,200	80	Pus tube.
74	29	F.	....	7,900	80	August 4th.
				7,500	....	August 5th.
				12,200	....	August 6th.
				14,300	....	August 7th.
				9,400	....	August 9th.
				10,200	....	August 11th.
75	23	F.	472,000	7,500	....	Pus tubes (small, size of finger).
76	..	F.	5,840,000	7,200	....	Pus tube.

PUS TUBE, PELVIC ABSCESS, AND PELVIC PERITONITIS.

White Cells.	Cases.
Between 7,000 and 10,000	11
" 10,000 " 12,000	9
" 12,000 " 14,000	8
" 14,000 " 16,000	9
" 16,000 " 18,000	8
" 18,000 " 20,000	10
" 20,000 " 22,000	8
" 22,000 " 24,000	6
" 24,000 " 26,000	4
" 26,000 " 28,000	4
" 28,000 " 34,000	5
" 34,000 or more	4
	76

From these data, together with two hundred and nineteen other counts not here recorded, I conclude that increasing counts of leucocytes usually point to the need of an operation; stationary leucocytosis to a well walled-off abscess. The size of the count is a rough measure of the size of the abscess, and patients *without* leucocytosis rarely need operation and usually recover under palliative treatment, as also do many *with* leucocytosis.

Differential Diagnosis.

Pelvic pain and soreness may be as great in various non-suppurative conditions (ovarian neuralgia, etc.) as when abscess is present; but the leucocyte count is raised in none of the pelvic disorders of women except in abscess, septicæmia (puerperal, after abortion, etc.), and hemorrhage (menorrhagia, metrorrhagia, ruptured tubal pregnancy). Endometritis and cystitis usually cause no leucocytosis. The application of these rules will not infrequently help in the diagnosis of pelvic disease and in deciding how much importance to attach to the complaints of pain, tenderness, etc., in a doubtful case. The absence of leucocytosis makes us rightly confident that no abscess of any considerable size exists.

OTITIS MEDIA.

Most cases, if purulent, show leucocytosis both before and after paracentesis. If serous (see Table XXVIII., cases 9, 17, 18, 21, 23) the count is usually lower, and we can predict with moderate certainty whether serum or pus will be found on puncturing the drum. When the mastoid is involved the count runs higher. If the case drags on, the hæmoglobin may get low, otherwise the red cells are not affected.

TABLE XXVIII.—OTITIS MEDIA.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	6	F.	....	36,700	..	Nephritis acuta. April 30th.
				27,300	..	May 7th.
				34,400	..	May 14th, otitis only.
				27,000	..	May 22d.
				21,000	..	May 28th, slight discharge still.
2	15		....	25,000	90	January 22d.
				12,000	..	" 27th.
				34,000	..	" 31st.
				24,000	..	February 2d.
				8,000	..	" 4th.
3	2	M.	....	23,000	55	
4	19	..	....	21,900	..	Ninth, T. 103.6°.
				13,200	..	Eleventh, T. 101°.
				10,800	..	Fourteenth, T. 99°.
5	6	M.	... .	18,600	20	
6	20	..	....	17,000	..	With jugular thrombosis.
				21,900	..	Third day.
7	25	..	....	15,000	90	
8	45	M.	....	14,500	..	With cerebral abscess.
9	Adult.	M.	4,786,000	16,800	..	Serous.
10	47	F.	4,168,000	16,600	65	Double purulent; vent not free; mastoid sore.
11	19	F.	5,120,000	16,480	88	April 28th.
				8,800	49	May 5th, well.
12	27	..	....	15,800		
13	Adult.	F.	5,942,000	15,200	..	Pus.
14	"	F.	4,472,000	14,750	60	December 7th, hysteria.
			5,416,000	9,750	46	December 25th (during dyspnœic and cyanotic attack).
15	24	..	....	14,200	72	
16	9	..	....	13,900		
17	32	..	....	12,000	..	Serous.
18	24	..	4,472,000	11,200	20	Serous.
19	22	..	....	11,000		
20	24	..	....	10,400	85	Catarrhal.
21	27	F.	4,850,000	8,500	69	Serous.
22	7	F.	4,416,000	6,400	..	Catarrhal.
23	Adult.	F.	4,100,000	4,000	..	Serous.
24	4	M.	....	Marked leucocytosis.	..	Purulent; chronic right, acute left. Diff. 116 cells; polymorphonuclear cells, 57%; lymphocytes, 31; eosinophiles, 3.

In some cases the blood alone enables us to distinguish otitis and its effects from typhoid. In a case recently examined which several excellent clinicians pronounced typhoid, though there was a marked leucocytosis and no serum reaction, the autopsy showed pus in the jugular and lateral sinus but no typhoid.

OSTEOMYELITIS.

In five cases in which no external opening was present, the patient complaining only of pain in the bone, the counts of leucocytes were 29,600, 25,600, 24,310, 23,400 and 18,000; in each the prediction that pus would be found was verified at operation. Three differential counts in chronic cases with sinuses showed nothing remarkable, no increase of eosinophiles and no myelocytes.

The diagnostic value of the blood in osteomyelitis seems to me considerable, inasmuch as it is difficult by the symptoms alone to feel sure enough of the existence of pus to be willing to operate. "Rheumatic pains," "growing pains," and neuralgia can be excluded by the presence of leucocytosis.

Other Abscesses.

(1) *Felon.*—It is striking to see how small a collection of pus can raise the leucocyte count. Patients with felons containing less than one-half drachm of pus may have a leucocytosis of 15,000 to 22,000. I have counted the blood in three such cases. The element of septicæmia must be considerable. It seems to make no difference whether or not the pus is under great *tension*. The leucocyte count does not fall sharply after the felon is opened, but gradually diminishes during the next seven to ten days. Even a

(2) *Gum boil* raised the white cells to 27,000 in one case. An

(3) *Abscess of the vulva* showed 23,500 leucocytes per cubic millimetre, and an

(4) *Abscess of the vagina* 12,800. Other varieties are:

(5) *Parotid abscess*, 45,500 leucocytes per cubic millimetre.

(6) *Subpectoral abscess*, 16,000 leucocytes per cubic millimetre.

(7) *Abscess of the neck*, 22,200 leucocytes per cubic millimetre

Carbuncle, 41,000 leucocytes per cubic millimetre.

(8) Peritonsillar Abscess—Six Cases.

Case.	Age.	White cells.	Per cent. Hæmoglobin.	
1	20	35,600	90	February 27th.
		16,300	..	March 3d.
2	33	26,000	75	
3	31	24,700	80	
4	31	19,700	65	June 17th.
		7,600	..	" 22d.
5	24	14,000	90	
6	30	13,000	80	

(9) *Psoas abscess* (infected), 50,000 leucocytes per cubic millimetre.

(10) *Abscess of ovary*, 26,000 leucocytes per cubic millimetre.

(11) *Suppurating Cyst of Ovary—Multilocular (Gangrene).* Age, 52; white cells, 62,400; per cent. hæmoglobin, 70, December 22d; white cells, 89,500, December 24th. Differential count: polynuclear, 94 per cent.; lymphocytes, 6 per cent.; eosinophiles, none. Autopsy.

(12) One case of *perinephritic abscess* was watched for some days while the patient was getting up strength for an operation. It was an abscess of several months' standing, not increasing in size during the last month, and the counts, as we should expect, did not rise or fall considerably, but showed a steady, well-marked leucocytosis.

July 29th, white cells, 21,400
" 30th, " " 21,200
August 8th, " " 22,400
" 11th, " " 23,000
" 24th, " " 22,200. (Operation.)

A second case counted showed only 16,000. Both abscesses contained over a quart of pus.

A third case, evidently tuberculous in origin and probably not much infected with pyogenic cocci, showed only 10,000 white cells per cubic millimetre.

(13) Two cases retropharyngeal abscess. Counts: Case I., 40,000; case II., 30,600.

(14) *Alveolar abscess*: Case I., 19,300; case II., 7,500.

(15) ABSCESS OF THE LUNG—NINE CASES.

Case.	Age.	White cells.	Per cent. Hæmoglobin.	
1	35	68,800	80	Death.
2	..	30,000		
3	14	17,000	85	January 9th.
		14,000	..	" 14th.
4	48	16,600	65	November 7th.
		7,400	..	" 9th.
		20,000	..	" 14th.
		11,900	..	" 16th.
5		16,800		
6	..	16,400		
7	..	16,000		
8	9	8,400	80	
9		5,100		

(16) SUBPHRENIC ABSCESS—FOUR CASES.

Case.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	4,450,000	53,267		
2	....	25,600	....	May 16th.
		15,500	....	May 17th.
		17,600	55	May 20th.
3	3,200,000	22,000	38	
4	....	15,300	....	October 20th. **Supposed typhoid for first week.**
		13,800	....	October 23d.
		16,600	....	October 27th.
		18,000	....	November 5th.
		22,500	....	November 10th. **Operation; a quart of pus; recovery.**

Diagnostic Value.

1. The patient with vulvar abscess was so morbidly modest that she complained of all parts of her body except the one diseased, and gave a train of symptoms which failed to account for the leucocytosis. The presence of this leucocytosis called for a much more searching physical examination than would have otherwise been made, and the seat of real trouble was discovered.

2. (*a*) The diagnosis between perinephritic abscess and cyst of the kidney is materially assisted by the fact that the former causes leucocytosis, while the latter (see page 371) does not.

(*b*) Both cancer of the kidney and perinephritic abscess cause leucocytosis, but if fibrin is not increased cancer is the more likely of the two. This differential mark has served me well in two cases.

(*c*) Hydatid of the kidney and pyonephrosis are not to be distinguished from perinephritic abscess by the blood examination. In abscess of the lung the blood gives no information that cannot be more easily gained in other ways.

3. Subphrenic abscess may be confounded with malignant disease, both of which may cause leucocytosis; but the absence of any increase of fibrin speaks against the existence of an abscess.

GONORRHŒA.

The red cells are not affected, but in acute cases a moderate leucocytosis is present and fibrin is increased. Qualitatively, the white cells have been said by Neusser and others to show an increased percentage of eosinophiles corresponding to the large proportion of these cells in the urethral discharge. Vorbach[1] has carefully studied twenty cases with reference to this point and finds the eosinophiles in the blood to vary from 0.5 to 11.5 per cent—averaging 4.2 per cent—within normal limits Bettman[2] and Pozzoli[3] found the eosinophiles usually increased, especially when the posterior urethra was involved. In one case with epididymitis the eosinophiles numbered 25 per cent.[4]

YELLOW FEVER.

Jones[5] found coagulation slow, the red cells *not* much diminished, but showing decided degenerative changes; hæmoglobinæmia is common. He makes no observations as to the white corpuscles. Pothier[6] of New Orleans, studying the epidemic of 1897, found the following results in 154 cases: The red cells were never considerably diminished; the leucocytes varied from 4,600 to 20,000—averaging about 9,000; hæmoglobin usually diminished at the height of the disease 50 to 75 per cent; normoblasts were noted in a few specimens.

A case recently observed at the Massachusetts General Hospital showed two days before death 7,800 leucocytes, 92 per cent of hæmoglobin, with an absence of the typhoid serum reaction. Through the kindness of Dr. Pothier I have been able to study cover-slips from twelve cases of yellow fever from the Charity Hospital of New Orleans. The differential counts of leucocytes are as follows:

	I.	II.	III	IV.	V.	VI.	VII.	VIII.	IX.	X.	XI.	XII.
Polymorphonuclear neutrophiles	77	74	93	86	87	88	97	84	86	84	77	73
Small lymphocytes	18	22	15	11	8	4	3	5	4	6	4	20
Large lymphocytes	5	2	2	2	5	8	..	11	10	6	18	6
Eosinophiles	..	2	..	.5	..	..	..	..	..	..	1	1
Myelocytes	..		..	.5	..	..	..	..	..	4		

Red cells showed nothing except in Case VIII., in which there were marked deformities and a few normoblasts. In some cases there was a marked leucocytosis, in others none.

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[1] Vorbach: Inaug. Dissert., Wurzburg, 1895.

[2] Bettman: Volkmann's Samml. klin. Vortr., No. 266, 1900.

[3] Pozzoli: Arch. für Derm. u. Syph., vol. xxiv.

[4] Archives for Derm. and Syphil., vol. 49.

[5] Journal of the American Medical Association, March 16th, 1895.

[6] Pothier: J. Am. Med. Assn., 1898, p. 885.

TYPHUS FEVER.

Ewing[1] in four cases found no leucocytosis. Tumas[2] found no leucocytosis, as the following case shows:

Date.	Day of disease.	Temperature.		Red cells.	Per cent hæmoglobin.	White cells.
		A. M.	P. M.			
January 4th.....	4th.	......	40.0			
" 5th.....	5th.	39.2	39.6	4,440,000	80	9,600
" 6th.....	6th.	39.0	39.5	4,220,000	77	4,800
" 7th.....	7th.	39.0	40.0			
" 8th.....	8th.	39.2	39.3	4,280,000	77	3,200
" 9th.....	9th.	39.0	39.5			
" 10th.....	10th.	38.8	39.2	4,440,000	77	3,200
" 11th.....	11th.	38.3	39.3			
" 12th.....	12th.	39.0	39.2	4,380,000	80	1,600
" 13th.....	13th.	38.8	39.5	4,780,000	80	3,200
" 14th.....	14th.	38.7	39.0			
" 15th.....	15th.	38.0	38.7	4,960,000	80	1,600
" 16th.....	16th.	38.1	38.8			
" 17th.....	17th.	38.7	38.6	4,160,000	70	4,800
" 18th.....	18th.	37.7	38.2			
" 19th.....	19th.	36.6	38.5	3,820,000	67	1,600
" 20th.....	20th.	38.1	38.3			
" 21st.....	21st.	37.5	38.1	3,450,000	62	3,280
" 22d.....	22d.	38.1	37.8	3,450,000	60	3,200
" 23d.....	23d.	37.5	38.0			
" 24th.....	24th.	37.4	38.0	3,130,000	50	3,200
" 25th.....	25th.	37.4	39.3			
" 26th.....	26th.	39.2	......			
Died on the 26th.						

On the other hand, Everard and Demoor,[3] and Wilks[4] found leucocytosis.

MALTA FEVER.

According to the article in Allbutt's recent "Text-book of Medicine" the red cells fall gradually in the course of the fever from 5,000,000 to about 3,500,000. Bruce finds the leucocytes normal in most cases. (See also page 538.) Bassett Smith[5] found a normal leucocyte count with relative increase of lymphocytes. Charles[6] makes the amazing assertion that at the height of the fever polymorphonuclear neutrophiles are entirely absent from the blood and only lymphocytes to be found. Musser and Sailer report a prolonged case with no important changes in the blood.

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[1] Ewing: New York Medical Journal, December 16th, 1893.

[2] Arch. f. klin. Med., vol. xli., p. 363.

[3] Annales de l'Institut Pasteur, February, 1893.

[4] Ref. in Sajous' Annual, 1895.

[5] Bassett Smith: Brit. Med. Jour., September 20th, 1902.

[6] Lancet, July 30th, 1898.

The serum reaction with the *Bacillus melitensis* was first observed by Wright of Netley and has been uniformly confirmed by all subsequent observers (*e.g.*, Musser,[1] Curry[2] in twenty-six cases, Kretz,[3] Aldridge,[4] Pascual,[5] and Bassett Smith[6]). The technique is described on page 538.

Bassett Smith considers the serum reaction valuable in *prognosis* as well as in diagnosis. His studies indicate:

(*a*) If the clumping power is low, and the symptom severe, the outlook is bad.

(*b*) If the clumping power is high and sustained the outlook is good.

(*c*) Cases with moderate symptoms and low clumping power are subject to repeated relapses, grave anæmia and chronic invalidism.

(*d*) Chronic relapsing cases with low *but gradually rising* clumping power ultimately regain full health.

GLANDERS.

Christol and Kiener[7] reported leucocytosis in glanders. In a fatal case of acute glanders with autopsy which was recently studied at the Massachusetts General Hospital the following counts were recorded:

October 24th, 1897. Leucocytes, 13,600; hæmoglobin, 100 per cent.
October 31st, 1897. Leucocytes, 11,600.
November 4th, 1897. Leucocytes, 13,000.
November 9th, 1897. Leucocytes, 12,000
November 12th, 1897. Leucocytes, 12,400.

Serum reaction absent; fibrin increased; pure culture of glanders bacilli from abscesses; 86 per cent of the leucocytes were polymorphonuclear; eosinophiles absent.

The bacilli of glanders can occasionally be cultivated from the blood.

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[1] Musser and Sailer: Phil. Med. Jour., 1898, p. 1408.
[2] Curry: Jour. Med. Research, July, 1901.
[3] Kretz: Lancet, 1898, vol. i., p. 221.
[4] Aldridge: Lancet, 1898, vol. i., p. 1394.
[5] Pascual: Rev. d. Cien. Med. d. Barcelona, 1903, No. 11.
[6] Bassett Smith: *Loc. cit.*
[7] Comptes Rendus de l'Acad. des Sciences, November 23d, 1868.

THE BUBONIC PLAGUE.

In 1895 Aoyoma, a Japanese observer, studied the blood of this disease.[1] He found the bacilli peculiar to the disease by cover-slip preparations from the blood. Ewing[2] found them by the culture in 90 per cent of cases near death, and in 60 per cent earlier in the disease (fifty cases). Aoyoma found the *red corpuscles* not altered except that their number per cubic millimetre was at times increased (*e.g.*, 7,600,000, 8,190,000). The cause of this I do not know, but it accounts for part of the leucocytosis. The *white corpuscles* showed a marked increase—20,000 to 200,000 (!) per cubic millimetre. Four cases showed counts over 100,000 and the average of six examined was 96,600. This leucocytosis was made up almost wholly of polymorphonuclear leucocytes; the eosinophiles were markedly diminished, and the blood plates were increased. The Austrian Plague Commission found only a moderate leucocytosis in most cases. Ewing (*loc. cit.*) found polynuclear leucocytosis in each of fifty cases, but no figures like those of Aoyoma. Coagulation is *very* slow (Alice Corthorn[3]).

Curry[4] found the presence of a leucocytosis of practical value in ruling out malaria, since the plague often begins with chills and other symptoms suggestive of malaria.

ACTINOMYCOSIS.

Ewing (*loc. cit.*) reports leucocytosis (21,500 in a single case affecting the lungs, and Schmidt gives the following:

Date.	Red cells.	White cells.	Per cent hæmoglobin.
October 6th	....	12,000	35
" 15th	3,170,000	14,500	
" 20th	....	19,700	
" 26th	3,200,000	22,900	38
November 4th	2,550,000	18,900	23

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[1] "Mittheilungen aus d. med. Fac. d. Kaiserlich Japanischen Universität," vol. iii., No. 2, Tokyo, Japan, 1895.

[2] Ewing: Med. Rec., April 4th, 1903.

[3] Corthorn: Brit. Med. Jour., May 10th, 1902.

[4] Curry: Boston Med. and Surg. Jour., March 21st, 1901.

In four cases of actinomycosis occurring at the Massachusetts General Hospital the following counts were recorded:

Case.	Location of the disease.	Leucocytes.	Remarks.
1...............	Liver............	31,700	June 18th, 1897.
		23,400	" 19th.
		23,200	" 25th. Autopsy.
2...............	Lungs............	20,900	April, 1897.
		23,000	August, 1899. Autopsy.
3...............	Liver	12,500	
4...............	Lungs	12,200	August 11th.
		21,000	" 15th.
		26,000	" 17th.

RABIES.

Courmont and Lesieur[1] found in three untreated cases of human rabies an increase in the polynuclear cells, accompanied in two of the cases by an increase in the total count. They state that the "Polynucleosis" is present from the beginning of the nervous symptoms, and its absence is strong evidence against the diagnosis of rabies. In other animals they got similar results. Their figures are as follows:

Case.	Red cells.	White cells.	Polynuclear.	Lymphocytes.	Hours before death.
1.....	5,300,000	24,800	88 per cent.	12 per cent.	1
2.....	....	increased.	84 "	16 "	5
3.....	....	5,000	84 "	16 "	29
		7,000	83 "	17 "	22
		12,000	85 "	15 "	8
		21,000	85 "	15 "	1

In three treated cases the blood was normal.

DENGUE.

H. Graham (*Med. Rec.*, February 8th, 1902) reports and pictures an unpigmented parasite in the blood of cases from an epidemic occurring at Beyrouth, Syria. His pictures are strongly suggestive of malarial parasites.

TETANUS.

In three (fatal) cases of tetanus treated with antitoxin, I observed the following counts:

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[1] Courmont and Lesieur Jour. de Phys. et Path. Gen., 1901, p. 600.

		White Cells.	Hæmoglobin.
Case I.	June 21st, 1897	11,100	70 per cent.
	June 23d, 1897	11,900	
Case II.		19,600	
" III	October 31st	18,200	80 per cent.

The eosinophiles do not decrease as in most fevers.

BERI-BERI.

In two afebrile cases seen at the Massachusetts General Hospital the following is recorded: Case I., red cells, 3,896,000; white cells, 7,800; hæmoglobin, 48 per cent. Case II., leucocytes, 25,900, March 6th; 10,600, March 7th; 14,000, March 16th. Differential count, March 16th: Polynuclear, 74.50; small lymphocytes, 18.25; large lymphocytes, 5.65; eosinophiles, 1.60.

The eosinophiles are said to be much increased in the acute stages. Spencer[1] states there is no leucocytosis. Ewing and Daubler, each in three cases, found normal leucocyte counts with moderate anæmia and no eosinophilia.[2] Wright[3] records the following:

No.	Age.	Stage of disease.	Type of disease.	Hæmoglobin.	Red cells.	White cells.	Result.
1	18	1st week	Acute pernicious	92	5,430,000	7,000	Fatal.
2	35	1st week	Acute pernicious	93	5,570,000	7,200	Fatal.
3	18	2d week	Acute pernicious	87	5,100,000	7,300	Fatal.
4	34	2d week	Acute pernicious	86	4,962,000	7,100	Fatal.
5	28	2d week	Acute pernicious	98	6,103,000	7,300	Fatal.
6	42	2d week	Acute pernicious	92	5,600,000	6,850	Fatal.
7	30	3d week	Acute pernicious	76	4,676,000	7,100	Fatal.
8	39	4th week	Acute pernicious	83	4,820,000	7,060	Fatal.
9	33	1st week	Acute	83	5,020,000	7,450	Recovered.
10	34	2d week	Acute	95	5,418,000	7,400	Recovered.
11	51	2d week	Acute	86	4,780,000	7,000	Paralysis persistent.
12	48	2d week	Acute	88	4,600,000	6,900	Recovered.
13	48	3d week	Acute	89	5,000,000	7,200	Recovered.
14	34	3d week	Acute	89	4,680,000	6,820	Recovered.
15	56	4th week	Acute	89	5,280,000	7,080	Paralysis persistent.
16	35	7th week		88	5,130,000	7,600	Recovered.
17	23	2d month		93	6,120,000	7,500	Recovered.
18	22	4th month		89	5,360,000	6,980	Recovered.
19	35	3d week	Beri-beri, residual paralysis	91	5,280,000	7,200	Paralysis persistent.
20	36	2d month	Beri-beri, residual paralysis	81	4,770,000	7,150	Paralysis persistent.
21	35	8th month.	Beri-beri, residual paralysis	93	5,176,000	6,980	Paralysis persistent.
22	36	9th month.	Beri-beri, residual paralysis	86	4,900,000	6,900	Paralysis persistent.
23	38	10th month.	Beri-beri, residual paralysis	92	5,670,000	7,600	Paralysis persistent.
24	..	12th month.		81	4,960,000	6,800	
25	..	12th month.		92	4,970,000	6,720	
26	..	6 years		87	4,896,000	6,900	

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[1] Lancet, January 2d, 1897.

[2] Bushnell has found leucocytosis in two cases (34,000 and 31,000) but with no increase in the per cent. of polynuclears (Lancet, October 10, 1903).

[3] Wright: "Studies from the Institute for Medical Research, Malay States," vol. ii., No. 1., 1902.

RELAPSING FEVER.

(See page 481.)

(*a*) *Diagnosis.* Leucocytosis is the rule. It is most marked just after the crisis. In countries where this disease is common the difficulty in diagnosing cases between attacks (when the spirochætes are absent from the blood) is frequently met with. Löwenthal has perfected a method by which in most cases the diagnosis can be made by means of the effect of the serum of suspected cases on the spirochætes of other active cases. The organism cannot be cultivated as yet, so that a diagnosis of this kind is possible only during epidemics when fresh blood containing the organism can be obtained. A drop of blood from the suspected case is mixed with a drop from a patient then undergoing a paroxysm, and the two are sealed with wax between slide and cover-glass and left in the thermostat for half an hour together with a mixture of normal blood and blood containing spirochætes as a control. At the end of that time, if the case be one of relapsing fever, the organisms in contact with the blood from that case *cease their motion*, while those in the control are lively. It is not a clump reaction but a direct bactericidal effect, which persists in the serum nearly up to the time of the next attack. The diagnosis so made by Löwenthal in forty cases was verified in every case by the course of the disease. In this way mild or abortive cases with few organisms in the blood can also be identified.

(*b*) *Prognosis.* If the above bactericidal power lasts as late as the seventh day from the last attack, and in sufficient intensity to immobilize the spirochætes in *one hour* or less, there will be no relapse. If these conditions are not fulfilled, relapse is sure to follow unless prevented by treatment. Löwenthal has verified this prognostic use of the serum in over one hundred cases.

CHAPTER V.

DISEASES AFFECTING THE SEROUS MEMBRANES.

TUBERCULOUS affections of serous membranes have been dealt with elsewhere (p. 301); but an exception was there made of pleurisy, for although there is reason to believe that the majority of cases of serous pleurisy are due to tuberculosis, we rarely have proof of it. Tuberculous cases have not always been distinguished from non-tuberculous. Hence the two are necessarily considered together here.

SEROUS PLEURISY.

Von Limbeck finds in non-tuberculous cases from 13,000 to 15,000 leucocytes per cubic millimetre. The red cells and hæmoglobin are not much affected except in chronic cases.

Rieder finds in non-tuberculous cases during the stage of fever moderate leucocytosis, 13,000 in one case in which the bacteriological examination showed the presence of Fraenkel's diplococcus in the exudation. After the fever has subsided the leucocytosis falls to, or nearly to, normal, so that cases examined for the first time some weeks after onset would show no increase at all. This he thinks explains the results of Halla and others who found no leucocytosis in serous pleurisy. According to Rieder the presence or absence of leucocytosis depends not so much on whether the product is serum or pus as on whether the trouble is stationary or advancing.

In tuberculous pleurisy despite fever Rieder found but 4,600 white cells in one case, and Pick got similar results in two cases.

Hayem makes no clear distinction of tuberculous and non-tuberculous cases, and states that "acute inflammatory" pleurisy has from 7,500 to 12,000 leucocytes per cubic millimetre. The fibrin network is much less dense than in pneumonia; in most of the tuberculous cases it is not increased at all.

Morse reports 224 counts in 20 cases of serous pleurisy—9 of them tuberculous. No relation could be established between the number of leucocytes and the presence, absence, or degree of fever, the presence of blood or microscopic pus in the fluid, the amount of fluid or the duration of the illness. Increase or decrease in the amount of fluid was not accompanied by any parallel change in the circulating leucocytes

Only 10 of the 224 counts were over 11,000, and 9 of these 10 were in a single case which was shown at autopsy to be complicated by a secondary pneumococcus infection Morse concludes that primary serous pleurisy does not show a leucocytosis. His figures are as follows:

From	3,000	to	4,000	2	counts.
"	4,000	"	5,000	19	"
"	5,000	"	6,000	40	"
"	6,000	"	7,000	31	"
"	7,000	"	8,000	50	"
"	8,000	"	9,000	42	"
"	9,000	"	10,000	27	"
"	10,000	"	11,000	8	"
"	11,000	"	12,000	4	"
"	13,000	"	14,000	1	"
Total				224	counts.

Fig. 31 from Morse shows how "the white count dodges up and down without the slightest apparent connection with the quantity of fluid."

In 314 cases examined at the Massachusetts General Hospital the count of leucocytes at the time of entrance was:

TABLE XXIX.—PLEURITIC EFFUSION (SEROUS).

Between	3,000	and	4,000	5	cases.
"	4,000	"	5,000	14	"
"	5,000	"	6,000	32	"
"	6,000	"	7,000	37	"
"	7,000	"	8,000	38	"
"	8,000	"	9,000	48	"
"	9,000	"	10,000	36	"
"	10,000	"	11,000	35	"
"	11,000	"	12,000	16	"
"	12,000	"	15,000	31	"
Over 15,000				22	"
Total				314	cases.

Average = 9,300.

Here tuberculous and non-tuberculous cases are not distinguished, and a majority of them were not seen till the trouble had been going on two or three weeks. The patients did not seek advice until the effusion was large enough to cause dyspnœa. Of the 242 cases all but 35 had *no leucocytosis.* Most of the cases were afebrile or nearly so. Eight cases reacted to injections of tuberculin. None of these 8 had leucocytosis.

The cases *with* leucocytosis were mostly those seen in the febrile stage, near the beginning of the sickness. No differential counts were made.

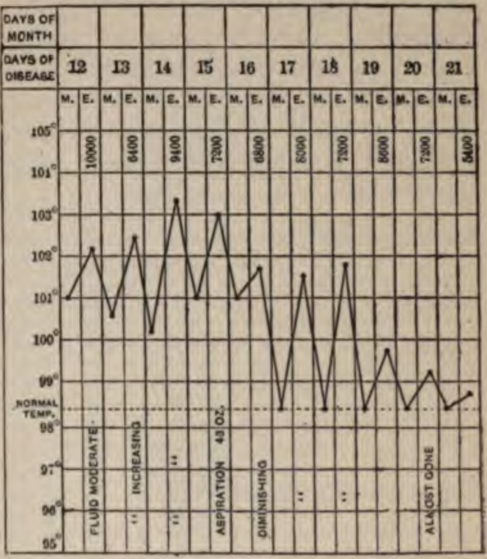

FIG. 31.—CHART OF LEUCOCYTES IN PLEURISY (MORSE).

In chronic cases the red cells are said to be considerably diminished, but this has not been the case in our series: no count of under 4,000,000 was recorded, and the coloring matter was not much diminished.

Summary.

1. Red cells and hæmoglobin show no important changes.
2. In adults the white cells are probably never steadily increased as a result of simple uncomplicated serous pleurisy. Occasional waves of leucocytosis occur in a small percentage of cases, but even then the leucocyte count rarely reaches 14,000. Continuous leucocytosis indicates some complication.

Diagnostic Value.

The blood count may help a good deal in doubtful cases by excluding empyema, pneumonia, and malignant disease of the lung, all of which are accompanied by high leucocyte counts. Compare the average count in serous pleurisy, 6,130, with the average in

pneumonia, 24,000, or in empyema, 18,300. The few counts I have seen of malignant disease of the lung have been still higher.

Hayem insists, rightly it seems to me, that clinicians could get real help from blood examination in almost every case of doubtful diagnosis in which the lung and pleura are in question. In children the leucocytes are sometimes considerably increased by even a serous inflammation, their blood reacting always more strongly than that of adults to any morbid influence, and in them it may be impossible to distinguish serous from purulent pleurisy.

DRY PLEURISY.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	24	....	30,000	95	
2	65	....	27,200	75	
3	24	....	22,200	90	
4	36	....	19,000	80	
5	31	....	16,200	85	
6	38	....	14,500	80	
7	21	....	12,000	90	
8	32	....	10,200	80	
9	41	....	9,000	72	
10	29	....	8,800	90	
11	25	....	8,700	85	
12	24	....	7,800	80	
13	31	... .	7,100	80	
14	21	....	2,700	85	

PURULENT PLEURISY (EMPYEMA).

The counts in twenty-six cases observed at the Massachusetts Hospital are as follows:

TABLE XXX.—EMPYEMA.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	12	..	....	57,800		
				54,400		
2	2	..	....	55,000	..	Streptococcus.
			5,440,000	49,200	51	
3	1	..	... .	45,500	..	Pneumococci in pus.
				37,700		
				31,700		
4	2	..	3,032,000	45,000	35	
				34,000	..	Fifth day.
				40,000	..	Eighth day.

Table XXX.—Empyema (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
5	4	..	....	44,000	..	First day.
				24,400	..	Third day.
				23,000	..	Fifth day.
				20,000	..	Eighth day. **Tap.**
				24,000	..	Eleventh day.
				31,400	..	Fourteenth day.
				22,000	..	Seventeenth day.
				41,500	60	
6	20	..	....	41,000	..	February 11th. **Tap.**
				29,900	..	February 15th. **Tap.**
7	21	..	....	38,000		
8	5	..	....	37,800		
9	32	..	....	35,600		
				35,200		
10	4	..	....	34,500		
			6,000,000	32,000		
11	4	..	....	30,400		
12	47	..	....	30,000	..	First day.
				39,000	..	Third day.
				27,000	..	Sixth day.
				26,000	..	Eighth day. **Pneumococci in pus**
13	38	..	....	30,000		
14	26	..	....	24,000		
				21,000		
				22,800	45	
				22,800	..	June 5th.
				34,700	..	June 7th.
				29,800	..	June 8th. **Tapped turbid serum.**
				17,700	..	June 9th.
				22,000	..	June 10th.
				22,100	..	June 12th.
				21,800	..	June 14th.
				17,200	..	June 22d.
				27,300	..	June 24th.
				30,100	..	June 29th.
				25,800	..	July 8th.
				22,600	..	Pneumococcus.
15	6	..	....	21.600	..	Pneumococcus.
				34,500	..	Five days later.
				20,600	..	January 5th.
				14,700	..	January 7th.
				11,400	..	January 23d.
				11,700	..	January 26th. **Tapped.**
				18,000	..	January 30th. **Re-accumulation.**
				26,000	..	February 3d. **Operated ; pneumococci and streptococci.**
16	2	..	....	19,600		
17	45	..		18,700	..	Friedländer's **bacillus.**
18	6	..		16,900	..	Tap. pus.
19	24	..	4,152,000	15,000	45	Operated.
20	27	..	....	14,200		
21	39	..	....	13,300	..	Gangrene of lung **also.**

TABLE XXX.—EMPYEMA (*Continued*).

No.	Age	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
				14,900	..	Fifth day.
				22,800	..	Fifteenth day.
22	30	..	....	13,000		
23	8	..	....	13,000	..	Sterile.
24	22	..	....	12,700	..	Tuberculous.
			4,192,000	10,800	48	December 20th.
				18,500	..	December 22d. **Broke into lung; cultures sterile.**
				14,500	..	January 2d.
				18,300	..	January 4th.
				10,000	..	January 9th.
				16,200	50	Pneumococcus.
				15,500		
				15,200		
			4,500,000	14,000		
			4,850,000	12,650	85	
				12,450	60	
			4,000,000	12,000		
				11,700	44	Cultures sterile.
				10,900		
25	71	..	....	8,400	..	Three quarts sterile pus.
				7,600	..	Operated; several pints of pus; streptococci.
26	45	..	....	6,500		

EMPYEMA.

Between	2,000	and	12,000	8	cases.
"	12,000	"	14,000	6	"
"	14,000	"	18,000	4	"
"	18,000	"	20,000	5	"
"	20,000	"	24,000	5	"
"	24,000	"	40,000	11	"
"	40,000	"	60,000	8	"
Total				42	"

Average 26,000 +.

This is in marked contrast with serous pleurisy as above noted. Von Limbeck and Da Costa have noted the same thing.

"In a case of empyema in which tubercle bacilli were extremely numerous, the writer found moderate intermittent leucocytosis (maximum 18,000)." (Ewing.)

PERITONITIS.

A patient with serous pleurisy (non-tuberculous) is hardly ever in danger, while if the general peritoneal cavity is the seat of a like inflammation, recovery is almost out of the question.

This clinical difference is parallel to the difference in the blood condition. Any inflammation (non-tuberculous) of the peritoneum, whether serous or purulent, calls very large numbers of leucocytes into the peripheral blood. The only exceptions to this rule are those cases in which the organism is so overwhelmed by the disease that it offers no resistance. We have seen that this same effect is produced in the severest cases of pneumonia and diphtheria, and presumably it is true of many other infectious diseases in which the blood has been less carefully studied.

Almost all cases of general septic peritonitis show very marked leucocytosis, and the spreading of a localized process is always indicated by an increasing leucocytosis. But here and there it happens that the patient cannot react against the disease at all, and then the leucocytes are normal or diminished. This never occurs in empyema, because the system is never so overwhelmed by a septic process in the pleura. The fibrin network is increased in almost all cases. The following counts, all in fatal cases, illustrate these points:

TABLE XXXI.—GENERAL PERITONITIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	34	F.	4,860,000	54,000	......	Abscess of spleen (?).
2	Adult.	F.	7,000,000	32,000	......	Purulent; from appendix—myelocytes, 2 per cent.
3	15	..	....	28,000	......	General septic.
				23,000	......	Next day.
4	27	..	....	27,800	68	December 6th. Epigastric.
				23,000	......	December 11th.
			4,004,000	34,200	53	December 17th.
5	28	..	....	24,100	......	Pelvic, after abortion. Seventh.
				17,800	......	Fifteenth.
6	27	M.	5,317,000	24,000	75	Dysentery, with perforation.
7	22	..	....	23,200	......	Gastric ulcer; perforation; operation Death.
8	Adult.	F.	4,000,000	22,000	......	Chronic, purulent.
9	31	M.	....	19,000	......	Ruptured bladder.
10	Adult.	M.	....	16,000	......	Moribund.
11	29	..	....	13,000	......	First day. Rupture of gall bladder.
				25,800	......	Second day. Died.
12	21	M.	....	12,200	......	June 30th.
				9,000	......	July 2d. Autopsy.
13	32	..	....	11,000	......	October 27th. Circumscribed.
				8,300	......	November 2d.
14	26	..	....	7,400	......	July 19th.
				9,700	......	July 28th.
15	60	..	....	6,000		
16	Adult.	M.	6,000,000	6,000	......	Purulent; operation. Death.
17	52	F.	....	5,328	......	Obstruction; died in three days; autopsy.
18	Adult.	M.	5,760,000	5,300	......	Purulent. Death within 24 hours.
19	41	F.	6,840,000	4,600	95	" " " 24 "
20	....	..	....	Marked increase.	......	After appendix operation. Diff. 1,000 cells: Polymorphonuclear cells, 90.5 per cent; lymphocytes, 9.5; eosinophiles, 0; myelocytes, 1.
21	38	F.	....	1,700!	......	August 2d. Autopsy.
				2,100!	......	August 3d.
22	27	..	....	1,600	......	General. Gastric ulcer.

Diagnostic Value.

1. When a diagnosis rests between peritonitis and (*a*) obstruction (non-malignant); (*b*) malignant disease; (*c*) hysteria, phantom tumors, or malingering, the presence of marked leucocytosis with increase of the fibrin network speaks strongly in favor of peritonitis.

Obstruction or malignant disease may increase the number of leucocytes but rarely increases the amount of fibrin.

Hysterical or malingering patients have normal blood.

2. We cannot distinguish serous from purulent peritonitis in septic cases, but *tuberculous peritonitis* can always be excluded if leucocytosis is present

3 As to the "chronic granular peritonitis," non-tuberculous and non-septic, I have seen no reference in hæmatological literature and have no first-hand knowledge.

4. In the *worst* cases leucocytosis may be absent, as in the most virulent type of pneumonia.

PERICARDITIS (WITH EFFUSION).

As in most other inflammations of serous membranes, we can distinguish the tuberculous cases which have no leucocytosis from the rheumatic or septic cases which always increase the white cells. The tuberculous cases are discussed under tuberculosis (see page 288). The following counts illustrate the rheumatic form of the disease:

TABLE XXXII.

Case.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	..	....	42,400	......	November 3d, 1895.
			32,600	......	November 7th, 1895.
			19,200	......	November 11th, 1895.
			17,500	......	December 8th, effusion nearly gone.
2	..	2,632,000	21,600	45	December 24th, endopericarditis, chronic nephritis.
			27,100	......	December 26th.
			36,600	......	December 29th, no fever.
			26,700	... ..	May 1st.
			19,200	......	May 3d.
			24,800	......	May 4th.
			28,600	......	May 7th.
			20,100	......	May 8th.

TABLE XXXII (*Continued*).

Case.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
3	..	4,568,000	26,000	67	December 14th
4	..	....	19,400	......	December 20th, effusion subsiding.
5	..	....	24,000		
6	..	4,168,000	19,447	67	
7	..	....	15,400		
8	..	....	14,600	65	Autopsy.
9	..	....	12,000	63	Tapped.
	22	4,376,000	17,680	58	February 28th.
			12,500	......	March 3d.
10	8	4,296,000	13,400	52	December 26th.
			18,900	.....	December 30th.
			15,800	53	January 15th.
			12,600	68	February 9th.
11	21	....	6,300	62	

Hayem has noted that pericarditis is far more apt to produce leucocytosis than is endocarditis.

DRY PERICARDITIS.

Case.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	11	....	34,600	80	Adhesions. Autopsy
2	39	....	31,800	80	March 31st.
			18,600	..	April 9th.
			22,000	..	April 22d, dry pleurisy, death
3	11	....	20,600	80	March 12th.
			25,000	..	March 13th, general septicæmia, pleurisy with effusion, alcoholism. Autopsy.
4	15	....	11,800	76	February 5th, mitral regurgitation.
			19,900	..	February 7th, cardiac hypertrophy
			1,850	..	February 15th, perinephritis.
			16,900	..	February 27th, enlarged liver, ascites.

HÆMOPERICARDIUM.

White cells.	Per cent hæmoglobin.	Remarks.
13,000	70	August 20th, tapped; bloody fluid obtained, discharged well.
14,200	....	August 22d.
10,400	....	August 24th.
15,100	....	August 27th.
7,200	....	August 28th.

MENINGITIS.

Leucocytosis is usually well marked. Von Limbeck considers that tuberculous meningitis can be distinguished from purulent by the absence of leucocytosis in tuberculous cases, but Osler[1] states that many cases of tuberculous meningitis *do* have leucocytosis throughout their course, and my own observations (see Table XXXIII.) confirm this. Of Rieder's cases one had leucocytosis and one did not. Zappert's case had 11,130 white cells, and Ziemke had one with 17,500. It seems, therefore, that we sometimes have here an exception to the rule that tuberculous processes do not produce leucocytosis. Certainly some cases do follow this rule. But however this may be, it is certain that purulent meningitis, whether secondary or of unknown origin, is characterized by high leucocyte counts, and if in a case evidently of meningitis of some kind leucocytosis is absent, the case is probably tuberculous in origin.

TABLE XXXIII.—MENINGITIS—OF VARIOUS TYPES NOT EPIDEMIC.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	19	..	....	62,000	..	Autopsy; pneumococcus.
2	Adult.	M.	5,900,000	40,000	..	Diff. 1,000 cells· adult cells, 93 per cent; young cells, 7 per cent; eosinophiles, 0
3	....	M.	6,400,000	33,000	..	(Otitis?) question of typhoid.
4	38	..	....	33,000	90	February 13th.
				36,400	..	February 17th, death.
5	1	..	....	32,000	90	Cerebro-spinal; death.
6	23	M.	6,000,000	27,500	95	March 16th; cerebro-spinal.
				16,500	..	March 18th.
7	37	..	....	27,000	.	Autopsy; pneumococcus; otitis media purulenta.
8	48	..	....	25,600	80	Subacute cerebro-spinal; March 2d.
				22,000	..	March 5th.
				24,600	..	March 9th.
				26,200	..	March 13th.
				31,400	..	March 16th.
				26,000	..	March 19th.
				27,400	..	March 21st.
				22,000	..	March 27th.
				28,000	..	March 30th.
				26,400	..	April 3d.
				27,600	..	April 6th.

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[1] "Practice of Medicine," 2d edition.

TABLE XXXIII.—MENINGITIS—OF VARIOUS TYPES NOT EPIDEMIC (*Continued*)

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
				18,600	..	April 10th.
				10,400	..	April 13th.
				7,600	..	April 16th.
				8,600	..	May 14th.
9	20	..	....	23,200	63	December 14th; cerebro-spinal.
				18,400	..	December 22d.
				14,300	..	December 24th.
				12,800	..	December 26th.
				8,000	..	December 28th.
				10,000	..	December 30th.
				10,000	..	January 1st
10	15	..	....	22,000	68	July 27th; cause unknown.
				19,000	..	July 29th; temperature 102.2°
				20,000	..	July 31st
				38,000	..	August 3d; temperature 103°.
				32,000	..	August 5th.
				26,000	..	August 7th.
				27,000	..	August 9th.
				22,000	..	August 12th.
				24,000	..	August 13th.
				26,000	..	August 18th.
				27,400	..	August 19th.
				25,500	..	August 21st.
				20,000	..	August 26th.
						Death September 5th; no autopsy.
11	36	..	....	20,800	75	
12	4	..	....	19,800	62	Autopsy; pneumococcus.
				19,900		
13	15 mos.	F.	5,020,000	19,500	73	
14	32	..	....	19,000	85	Cerebro-spinal: April 11th.
				13,000	..	April 16th.
				28,400	..	April 23d.
				31,200	..	April 26th.
				18,000	..	April 29th.
				11,200	..	May 2d.
15	34	..	....	18,500	..	Cerebro-spinal
16	4	..	....	16,400	64	Lumbar puncture shows diplococcus intercellularis of Weichselbaum. Death.
17	7	M.	....	16,000		
18	26	M.	....	16,000		
19	20	F.	....	15,784	..	Autopsy; cerebro spinal
20	2	M.	....	14,200	..	Basilar: no tuberculosis in family; had pneumonia.
21	22	M.	4,356,000	14,000	72	
22	27	..	....	13,200	85	Cerebro-spinal, March 28th.
				15,600	..	Death, March 30th.
						Different counts 500 cells, polynuclear leucocytes, 83.8 per cent; small lymphocytes, 11.4 per cent; large lymphocytes, 4.8 per cent.

TABLE XXXIII.—MENINGITIS—OF VARIOUS TYPES NOT EPIDEMIC (*Continued*)

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
23	10	..	... .	12,800	85	January 24th.
				18,600	..	January 26th.
				10,000	..	February 3d.
24	35	M.	....	11,700		
25	40	..	....	9,600	70	Autopsy; chronic diffuse pachymeningitis.
26	32	..	....	8,000	95	Cerebro-spinal; death.
27	16	..	....	7,200		

EPIDEMIC CEREBRO-SPINAL MENINGITIS.

Williams finds leucocytosis in about two-thirds of his cases.

The following counts were made during the epidemic of 1897. The red cells are not markedly affected. Vasomotor polycythæmia may occur. Leucocytosis is the rule, but is not invariable. In a general way the higher the count the severer the case, and the count usually rises as the case gets worse and falls with improvement, though often very slowly. In the febrile recrudescences so common in chronic cases, the leucocytes usually rise again, though the eosinophiles may not disappear as they ordinarily do in the earliest days of the illness. No prognostic inferences can be drawn from the behavior of the eosinophiles in meningitis.

TABLE XXXIV.—EPIDEMIC CEREBRO-SPINAL MENINGITIS.

White Cells.	Counts.
Between 5,000 and 10,000	9
" 10,000 " 15,000	50
" 15,000 " 20,000	42
" 20,000 " 25,000	27
" 25,000 " 30,000	21
" 30,000 " 35,000	9
" 35,000 " 40,000	10
" 40,000 " 45,000	7
" 45,000 " 50,000	1
" 50,000 " 55,000	5
Total	181

Flexner and Barker, investigating a large epidemic at Lonaconing, Md., found leucocytosis in every case (12,000–32,000 per cubic millimetre). The epidemic studied by Williams and myself was apparently due to the diplococcus intracellularis of Weichselbaum. Secondary meningitis (otitis media, etc.) seems to have similar effects on the blood.

Diagnostic Value.

Meningitis is the only intracranial disease (except abscess and apoplexy) which shows leucocytosis, and this fact may be of great help in excluding other causes of coma.

1. Brain tumor, hysteria, lead encephalopathy, and most cases of narcotic or alcoholic intoxication do not cause leucocytosis and hence can be excluded by its presence.
2. Uræmia, apoplexy, sunstroke,[1] diabetic coma, and post-epileptic coma may have leucocytosis and cannot be distinguished from meningitis when leucocytosis is present; but the absence of leucocytosis excludes meningitis.
3. Some cases of typhoid, when seen for the first time and without a history of the previous illness, may be difficult to distinguish from meningitis, but typhoid never has leucocytosis if uncomplicated and meningitis always has.
4. From pneumonia we cannot distinguish meningitis by the blood count.

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[1] In a case of heat exhaustion (temperature 104°) without coma, a leucocyte count of 27,200 is recorded at the Massachusetts General Hospital.

PART III.

CHRONIC INFECTIOUS DISEASES.

CHAPTER VI.

TUBERCULOSIS.

AGGLUTINATIVE REACTION.

SINCE Arloing and Courmont's communication in 1898 at least nineteen other observers have studied the question whether there is an agglutinative reaction between the blood of tuberculous patients and tubercle bacilli dissociated in fish bouillon or other nutrient liquids. Their results have been admirably summarized by L. M. Loeb.[1] Thirteen of the nineteen observers (Russian, French, and German) get results practically identical with those of Arloing and Courmont, *i e.*, find agglutination in a considerable percentage of tuberculous subjects *and also in from 30 to 60 per cent of those showing no clinical evidence of tuberculosis.* This last fact deprives the test of practical value in the estimation of Loeb and of some others whose results are the same as those of Arloing and Courmont.

At least six investigators, among whom are Beck, Koch, and Fraenkel, fail altogether to confirm Arloing and Courmont's results. I have no personal experience with the test.

RED CORPUSCLES AND HÆMOGLOBIN.

(*a*) *Quantitative Changes.*

I. The striking fact is the absence of such anæmia as we should expect, judging from the pallor of the patients and the nature of the disease. It is common to find a normal or even increased number of red cells in pale, cachectic-looking consumptives. We cannot help wondering whether our methods of examination are at fault, that is, whether the drop we examine is typical. (For discussion of the subject see page 68.) However this may be, it is undoubtedly the fact that in most cases of tuberculosis, even in advanced stages, the count of red cells is often *normal, or increased with correspondingly high hæmoglobin.*

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[1] Loeb. Jour. Am. Med. Assn., May 23d, 1903 (literature).

II. In a smaller number of cases the hæmoglobin is much diminished, although the count of red cells is normal—in other words, we find the blood characteristic of a moderately severe secondary anæmia. The red cells are numerous enough, but only because their numbers have been recruited by the influx of "half-baked" or decrepit corpuscles, small-sized and pale, poor in albumin and hæmoglobin.

The condition differs from that of chlorosis mainly in that some of the red cells are normally developed and nourished, while in chlorosis all, or nearly all, are feeble. Such blood occurs in the severer and more cachectic sufferers from tuberculosis, just often enough to make us wonder that it is not *always* to be found.

III. In a small percentage of cases both red cells and hæmoglobin are considerably diminished, the latter usually suffering more than do the actual number of cells, that is, the color index is usually below 1.

Von Limbeck[1] has recorded a case in which in the course of a tuberculous process (acute) the red cells fell as low as 700,000 (white cells, 6,000; specific gravity 1.032). But the account of the blood is not sufficiently explicit in this case to enable us to exclude a true pernicious anæmia in the course of which the tuberculosis may have been only the last incident. No other such case is on record, so far as I am aware.

"In phthisis, as well as in other tuberculous processes, great caution must be used in judging of the patient's improvement from an increase in red cells or hæmoglobin. The writer has seen the hæmoglobin and red cells increase while the patient was rapidly losing flesh, the lesions advancing, and the total quantity of blood doubtless falling. In several of Bierfreund's cases the hæmoglobin steadily increased while the patient was developing general tuberculosis." (Ewing.)

IV. *Fibrin* is not increased unless extensive secondary infection is present.

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[1] *Loc. cit.*, p. 564.

(*b*) *Qualitative Changes.*

I There may be none whatever.

II There may be only a pallor of some of the individual corpuscles with slight changes in size and shape.

III In very severe cases the poikilocytosis may be extreme, but this is much rarer than in many other cachexias of the same severity (*e.g* , malignant disease)

IV An important point is the usual absence of nucleated red cells Even after hemorrhages it is rare to find any nucleated red cells, and this is in marked contrast with cancer cases, in which nucleated red cells are the rule.

V. The degenerative changes described by Maragliano are sometimes found in severe cases with mixed infection (*vide infra*)

As regards the influence of the different seats of tuberculous disease (meningeal, pulmonary, genito-urinary, acute miliary, etc.) upon the red corpuscles and hæmoglobin the following are the probabilities:

Pure tuberculous disease itself, whatever its seat, has little or no effect upon the blood The widely different conditions of the blood found in different cases depend probably on the presence or absence of various other organisms (diplococcus lanceolatus, pyogenic cocci) associated with the tubercle bacillus, and on whether there is some drain on the body albuminoids (diarrhœa, peritoneal effusion, starvation, prolonged suppuration). When the infection is a mixed one, the blood shows the ordinary effects of septicæmia (for then the case *is* practically one of septicæmia) in lessening the number and quality of the red cells. When there is drain on the fluids and proteid constituents of the body, the red cells may not seem to be diminished, owing to the concentration of the blood from loss of fluid Under such circumstances they may even seem increased, but the individual corpuscles are sure to be lacking in hæmoglobin and the other nitrogenous bodies of which they largely consist.

Fever may be present without there being any changes in the red cells that we can detect. It is only septic fever, and not the fever of pure tuberculosis, that drains the corpuscles of their vitality and lowers their numbers.

LEUCOCYTES.

(*a*) *Quantitative Changes.*

Here, as with the red cells, the striking fact is the absence of changes in pure tuberculosis. It makes no difference whether we are dealing with tuberculosis of the bones, serous membranes, or internal organs. So long as the infection remains unmixed the white cells are not increased. In certain localities (lungs, kidneys) the opportunities for a secondary infection and septicæmia are so great that we frequently find evidence of it in the blood. On the other hand, psoas abscesses before they are opened often contain only tubercle bacilli, and the blood of such cases shows no considerable changes.

So much more is known of the numerical variations of the leucocytes in tuberculosis than of the other blood constituents, that I shall give a separate account of them in phthisis, in tuberculous bone disease, in tuberculous meningitis, acute miliary tuberculosis, genito-urinary tuberculosis, and tuberculous peritonitis.

I. PHTHISIS.

I. In *incipient phthisis* the leucocytes are normal except after hæmoptysis.

II. After attacks of *hæmoptysis*, there is usually leucocytosis, subject to wide variations according to the amount of the hemorrhage and the resisting power of the patient. This follows the laws of ordinary post-hemorrhagic leucocytosis (*vide supra*) and disappears quickly when the hemorrhage ceases.

III. *Cavities.*—Very constantly accompanied by leucocytosis. Indeed the absence of leucocytosis in any case proves the absence of any cavity of considerable size.

Ewing "has seen both lungs consolidated and riddled with small cavities in a case lasting five weeks, yet the leucocytes were never found above 12,000. The absence of leucocytosis in these cases of acute phthisis, which resemble pneumonia, may often be of value in diagnosis. Similarly, in a case of subacute empyema in which the tubercle bacillus was largely concerned, the leucocytes were found not to exceed 14,000 during an acute febrile period." In moderately advanced cases living in the open air with ample proteid diet, Galbraith[1] finds "moderate leucocytosis, large absorptive lymphocytosis, and an almost constant eosinophilia."

IV. *Extensive infiltration* ("tuberculous pneumonia") may cause marked increase of white cells, sometimes as great as in croupous pneumonia, but this is not invariable.

V. *Fibroid Phthisis* (chronic interstitial pneumonia).—As a rule the leucocytes show no increase, but if, as sometimes occurs, we have the combination of this condition with cavity formation, the latter may increase the count of white cells.

VI. *Fever.*—When the temperature is normal, the leucocytes are normal, but a febrile state may or may not be accompanied by leucocytosis (according, presumably, as the fever is or is not due to pyogenic organisms).

VII. *Tuberculin Injections.*—At the height of the reaction fever the leucocytes almost always rise, the lymphocytes and eosinophiles being relatively increased.

In a general way, the worse the case the higher the leucocyte count, yet the signs may be advanced without causing any leucocytosis if cavities are absent.

The following tables give some idea of the range of the counts in average hospital cases of phthisis:

PHTHISIS—RED CELLS.

Between 2,000,000 and 3,000,000 = 1 case.
" 3,000,000 " 4,000,000 = 22 cases.
" 4,000,000 " 5,000,000 = 27 "
" 5,000,000 " 6,000,000 = 17 "
Total........................ 67 "

PHTHISIS—HÆMOGLOBIN.

From 10 to 20 per cent = 1 case.
" 20 " 30 " = 0 "
" 30 " 40 " = 5 cases.
" 40 " 50 " = 8 "
" 50 " 60 " = 21 "
" 60 " 70 " = 35 "
" 70 " 80 " = 38 "
" 80 " 90 " = 19 "
" 90 " 100 " = 5 "
Total............. 132 "

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[1] Galbraith: Brit. Med. Jour., March 14th, 1903.

Phthisis—White Cells.

Between 3,000 and 4,000 = 5 cases.
" 4,000 " 5,000 = 7 "
" 5,000 " 7,000 = 25 "
" 7,000 " 9,000 = 26 "
" 9,000 " 11,000 = 27 "
" 11,000 " 15,000 = 48 "
" 15,000 " 20,000 = 29 "
" 20,000 " 30,000 = 14 "
" 30,000 " 40,000 = 4 "

Total ....185 "

The number of those showing leucocytosis is slightly greater than those without it, probably because incipient cases rarely think themselves sick enough to come to a hospital. On the other hand, some of the cases which appear to have been going on for months have normal leucocyte counts. The duration is less important than the nature and severity of the process. It is rare to see extensive signs in the lungs without leucocytosis—fibroid phthisis excepted

Qualitative Changes in the White Cells

1. Many cases show none at all.
2. When the leucocyte count is normal we may find an increased percentage of large and small lymphocytes, such as is commonly found in any blood poor in nutritive qualities (see page 89)
3. When leucocytosis is present, we usually find the ordinary marked increase in the percentage of polymorphonuclear cells at the expense of the lymphocytes.

For example: C. D——, male, thirty-two years old. Tuberculosis of lungs, with cavities; leucocytes, 17,580. Differential count of 1,000 cells shows:

	Per cent
Polymorphonuclear	83.4
Lymphocytes (small)	8.2
Large lymphocytes (large and transitional)	8.4
Eosinophiles	0.0

4. Eosinophiles are increased during the reaction from an injection of tuberculin, and also in some cases with cavities in which possibly the individual inoculates himself with tuberculin manufact-

ured in the cavities of his own lungs. In most cases associated with leucocytosis they are absent.

5. Myelocytes were found by Holmes, W. R. May, and myself in many cases of advanced phthisis. They averaged 0.3 per cent.

Other Changes.

Neusser and his followers have advanced a theory that the occurrence of perinuclear basophilia[1] during tuberculosis is a favorable sign and marks a system capable of resisting the tuberculous infection The researches of Futcher and my own attempts to verify Neusser's theory have not confirmed his findings.

Holmes, of Denver, has studied the leucocytes in phthisis with great care and considers that he finds therein means not only of diagnosing tuberculosis by the blood alone, but of measuring the degree of advancement of the process and the amount of resisting power in the patient.

I have carefully followed out Holmes' procedures with stains seen and approved by him. I can verify most of his statements of fact, but some of the inferences which he draws therefrom are, I think, wholly unwarranted The blood changes in pulmonary tuberculosis are mainly such as he describes, but they have no diagnostic value, as similar changes are found in a great variety of other diseased conditions. The increase of polymorphonuclear forms in advanced cases, the increased amount of "débris," the degenerating forms, etc , are all characteristic not of tuberculosis alone, but of any severe suppurative process The increase of "débris" is probably the same datum which Watkins interpreted as an increase in blood plates and Goldberger and Weiss as "extracellular glycogen." (With Holmes' "undeveloped nuclei" in the leucocytes, compare page 102)

II. BONE TUBERCULOSIS.

Brown[2] has studied seventy-two cases, Dane[3] forty-one. Dane's study of the blood in forty-one cases of hip disease and Pott's disease is a very careful one. Whenever abscesses appeared in connection with the disease, cultures were taken when the abscess was first opened and again later on, and the coincidence of low counts with absence of pyogenic cocci and with high counts of secondary pyogenic infection is very notable. Dane's conclusions are as follows.

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[1] See Appendix.

[2] Transactions of California Medical Society, 1897.

[3] Boston Medical and Surgical Journal, May 28th, 1896.

1. "High leucocyte counts, especially in hip disease, point to the probability that there is, or soon will be, abscess formation; but low counts do not preclude the presence of abscess, especially in long-standing cases.

2. "If abscess is present, a low count of white cells indicates the absence of secondary pyogenic infection (proved by cultures).

3. "Cases of traumatic origin are generally accompanied by a high leucocyte count.

4. "The leucocyte count bears no direct relation to the temperature; one case with 30,980 leucocytes (five-year-old girl) showed a temperature of only 99.4° at the time of the count. In another girl of three years whose temperature ranged between 101° and 104°, the leucocytes were only 7,224, or subnormal for that age (*vide infra*, page 512).

5. "Cases where at the primary operation the pus proved sterile show an increase in the leucocyte count when the wound becomes infected with pyogenic organisms" (as it always does).

6. "The red cells are rarely diminished, but the hæmoglobin is usually relatively low (mild secondary anæmia in these cases) This absence of a diminution in the red cells in these cases is the more remarkable because they were almost all in young children whose blood is much more sensitive to any deleterious influence than that of adults."

Brown dissents from several of Dane's conclusions. He thinks that a case may go on to abscess formation without any increase in the leucocyte count When an increase *does* take place, he thinks it due either to a secondary infection or to an increased activity of the tuberculous process itself without any secondary infection. The latter process, however, in Brown's experience causes only a moderate increase (2,000–3,000), while if a marked increase suddenly or gradually occurs he thinks it "most significant of secondary infection." With Dane's fifth conclusion he wholly agrees and adds: "After the infection (produced by the operation) the leucocytosis is very high for a time, and if the sepsis is acute and threatens life, it remains high until the crisis is passed." Otherwise it gradually falls after the first few days, and if the patient progresses well, it disappears. If the pyogenic matter overcomes the recuperative power, ucocytes fall as in peracute pneumonia or peritonitis. In such the anæmia increases as well.

Qualitative Changes.

(*a*) As in other forms of tuberculosis there may be none at all.

(*b*) The cell-changes in purely tuberculous cases are illustrated well by Case 17 of Dane's series, a boy of seven whose blood on the day of operation for hip disease with large abscess showed 8,932 cocytes The differential count was as follows:

	Per cent.
Polymorphonuclear neutrophiles	40
Small lymphocytes	49
Large lymphocytes and transitional forms	8
Eosinophiles	3

Eight ounces of pus were evacuated, in which cultures showed the absence of pyogenic organisms

This case demonstrates that some cases of tuberculous suppuration have no tendency to produce leucocytosis or to increase in the neutrophiles, but influence the blood only by producing what might be termed a functional debility of the blood through lack of nutritive substances in the plasma This condition is by no means peculiar to tuberculosis, but occurs in a great variety of debilitated or cachectic conditions, as already stated

(*c*) But when a septicæmia complicates the tuberculosis, cell metamorphosis appears to be accelerated, and we get with the quantitative increase of leucocytes such qualitative changes as the following:

	Per cent.
Polymorphonuclear neutrophiles	84
Lymphocytes (small)	9
Lymphocytes (large and transitional)	6
Eosinophiles	1

This was a case (No. 33 of Dane's series) in which the abscess, sterile when first opened, had become inoculated with the staphylococcus aureus.

(*d*) Not every case with leucocytosis shows qualitative changes as the above. One of Dane's cases (No. 22, a boy of seven) showed a leucocytosis of 23,387, but only sixty per cent of these were polymorphonuclear and two per cent eosinophiles.

In a case recorded by Dane (No 32), *tuberculous osteomyelitis* showed 6,083 white cells (subnormal, as the child was only two years old) with sixty-four per cent of polymorphonuclear cells. The pus from the bone cavity showed no pyogenic organisms on culture. Ordinary septic osteomyelitis gives very different results (see page 265). Dane's cases were almost exclusively hip and spinal affections.

The following cases from the Massachusetts General Hospital records illustrate tuberculosis of other bones:

TABLE XXXV.

Case.	Diagnosis.	Red cells.	White cells.	Per cent hæmoglobin.
1	Tuberculosis of the knee-joint...... ...	6,472,000	9,400	63
2	Tuberculosis of the knee-joint..........	2,704,000	8,000	?
3	Metatarsal tuberculosis	4,650,000	6,500	61
4	Tubercular rib.......................	5,016,000	5,800	73

III. ACUTE MILIARY TUBERCULOSIS.

Probably there are no important changes in the red cells or hæmoglobin. The number of cases on record is too small to enable me to speak positively on this point, but the acuteness of the disease would lead us to expect the normal or approximately normal conditions recorded in the few published cases.

About the leucocytes we know more

Quantitative Changes in the Leucocytes.

There were normal or subnormal counts in two-thirds of my cases. Sometimes the count is raised by a complicating pyogenic infection or by an extensive involvement of the meninges. In other cases the cause of the leucocytosis is obscure.

Warthin[1] reports a case with autopsy in which he made over thirty counts of the white corpuscles, verifying the more remarkable results by repetition. Autopsy showed, besides miliary tuberculosis, a cavity in the lower lobe of the right lung and a suppurating focus about the seminal vesicles containing four ounces of pus rich in tubercle bacilli. Whether pyogenic organ-

[1] Medical News, 1895.

isms were also present is not stated. The leucocyte counts were as follows:

TABLE XXXVI.

Day.	Hour.	Leucocytes.	Remarks.
December 6th	10 A.M.	3,500	
" 12th	8 A.M.	5,000	
" 18th	5 P.M.	3,500	
" 22d	10 A.M.	5,625	
" 22d	11·30 A.M.	4,725	
" 22d	3 P.M.	5,000	
" 22d	5 P.M.	3,125	
" 24th	8:30 A.M.	3,750	
" 24th	11:30 A.M.	3,750	
" 24th	2 P.M.	2,500	
" 24th	4:30 P.M.	2,500	
" 25th	8 A.M.	1,875	
" 28th	5·30 P.M.	3,750	Red cells, 4,125,000; hæmoglobin, 80%
" 29th	10 A.M.	1,250	
" 29th	2 P.M.	1,250	
" 29th	5:30 P.M.	3,750	
" 31st	12 M.	1,250	
" 31st	6 P.M.	2,500	
January 2d	11 A.M.	1,250	
" 2d	5 P.M.	2,500	
" 3d	2:30 P.M.	600	Severe chill. Count repeated several times.
" 5th	8:30 A.M.	3,750	
" 5th	11 A.M.	3,137	
" 5th	4 P.M.	8,125	Moribund.
" 6th	9 A.M.	10,000	
" 6th	10 A.M.	5,625	
" 6th	11 A.M.	2,500	
" 6th	12 M.	5,625	
" 6th	12:50 P.M.	Death.	

In another case he found also a subnormal count. Rieder found normal counts in two cases. Von Limbeck states that the leucocytes are normal, but gives no counts.

The following cases from the Massachusetts General Hospital records illustrate these points:

TABLE XXXVII.—ACUTE MILIARY TUBERCULOSIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	28	M.	2,448,000	550	85	March 8th.
				1,200	..	March 11th.
				7,100	..	March 11th, gave protonuclein gr. xv. t.i.d.

TABLE XXXVII.—Acute Miliary Tuberculosis (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
						March 13th, differential count: Polymorphonuclear, 78 per cent. Lymphocytes (small), 12 " Lymphocytes (large), 9 " Eosinophiles, 1 "
				1,300	..	March 14th, glands rapidly diminishing.
						March 18th, died. Autopsy.
			3,296,000	3,000	43	
2	57	..	4,424,000	2,200	85	August 20th.
				2,200	..	August 25th.
				4,700	..	August 27th.
				7,100	..	August 29th. Autopsy.
	24	..	....	3,300	..	First day.
				8,000	..	Third day.
				4,400	..	Ninth day.
				9,100	..	Twelfth day.
3	52	F.	....	3,500	90	
4	18	M.	....	3,600	..	Autopsy.
5	40	M.	....	3,750	..	Autopsy.
6	40	..	....	4,000		
7	14	F.	3,720,000	4,400	45	Autopsy.
8	26	..	....	4,600	..	First week.
				3,400	..	Sixth week.
9	51	M.	4,664,000	4,800	..	Autopsy. Chronic phthisis also.
10	23	M.	....	4,900	..	Autopsy. Differential count normal.
11	14	..	....	5,400	65	
12	18	F.	....	5,400	80	September 21st.
				7,400	..	September 24th. No serum reaction.
13	29	M.	....	5,600	64	Autopsy. No serum reaction.
14	12	F.	....	6,100	..	Autopsy.
15	19	F.	....	6,600	..	Autopsy.
16	56	..	....	6,800	..	First day.
				8,200	..	Ninth day.
				21,000	..	Day of death.
17	37	F.	....	1,500	71	Autopsy.
18	18	..	....	7,600	..	First day.
				8,600	..	Fourth day. Ninth, death.
19	36	M.	....	7,600	..	Healed phthisis also. Autopsy.
20	36	..	4,784,000	7,600	70	January 26th, differential count: Polymorphonuclear, 62 per cent. Lymphocytes, 37 " Eosinophiles, 1 "
				8,200	..	January 29th.
				7,200	..	January 31st. Autopsy.
	20	F.	....	7,800	..	May 14th.
				7,200	..	May 22d, death. Autopsy.
21	29	..	....	7,600	100	September 25th.
22	35	..	3,920,000	8,000	45	
				8,900	..	November 12th. Autopsy.
23	22	..	....	8,600	75	Tuberculous salpingitis; tuberculou meningitis.
24	30	..	4,500,000	8,800	52	
25	24	..	....	9,100	85	August 24th.

TABLE XXXVII.—ACUTE MILIARY TUBERCULOSIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
				14,000	..	August 25th.
				21,200	..	August 26th.
				8,600	..	August 28th.
				9,000	..	August 31st.
	30	M.	....	9,250	..	April 18th.
				9,450	..	April 20th. Autopsy.
26	45	M.	5,237,000	10,000	..	Autopsy.
27	38	..	....	12,200	..	Autopsy.
28	28	..	....	12,200	65	Death.
29	22	M.	....	12,700	..	Phthisis also. Autopsy.
30	20	..	....	13,200	80	March 15th.
				20,000	..	March 16th.
				20,200	..	March 17th.
				20,900	..	March 18th.
				24,700	..	March 20th. Autopsy. Tuberculous meningitis.
31	21	..	....	16,000	85	Autopsy.
32	6	..	....	19,800	83	October 29th.
				30,200	..	October 31st.
				22,000	..	November 1st.
				25,500	..	November 3d.
33	20	..	....	27,000	55	
34	44	..	....	30,000	90	Death.
35	78	..	2,416,000	32,000	29	Differential count 1,000 cells: Polynuclear, 87 per cent. Lymphocytes, 11 " Eosinophiles, 0 " Myelocytes, 2 " Normoblasts = 5. Megaloblasts = 2. Complicated with diphtheria.
36	14	..	....	36,000	..	Autopsy.

Case 1 of the above table is a striking example of the remarkably low leucocyte count sometimes seen in this disease The counts were carefully verified by several competent observers.

Qualitative Changes

In Warthin's case above quoted, he repeatedly made differential counts of the leucocytes by Ehrlich's methods, with this average result:

Polymorphonuclear neutrophiles...........	91.48	per cent.
Lymphocytes (small).....................	3.52	"
Lymphocytes (large and transitional).......	3.00	"
Eosinophiles.............................	0.00	"
Myelocytes..............................	2.00	"

The differential counts made in four of my cases showed no constant percentages.

IV. TUBERCULOSIS OF SEROUS MEMBRANES.

1. Tuberculous Peritonitis.

The blood condition is exactly as in other forms of tuberculosis, except in so far as it is modified by the drain exerted on the blood by diarrhœa or by transudation or exudation into the peritoneal cavity. Such events concentrate the blood by withdrawing water and albumin from it and may give us a normal number of red cells per cubic millimetre, when in reality a considerable anæmia is present. As a rule, the blood shows a mild secondary anæmia without leucocytosis or with leucopenia. This is exemplified in the following table from the Massachusetts General Hospital records:

Table XXXVIII.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	26	F.	3,120,000	2,240	58	
2	28	....	....	2,600		
3	33	F.	2,900,000	3,800	48	
4	24	M.	5,360,000	3,800	..	January 6th, 1896.
			5,760,000	5,600	85	April 13th, 1896.
5	25	F.	....	3,900	..	Tuberculous tube.
6	21	M.	... .	4,400		
7	25	....	....	4,700	52	
8	21	....	3,684,000	4.800	43	
9	27	M.	....	4,900	64	March 1st.
				5,500	..	March 9th.
10	43	M.	....	5,000	..	December 18th, 1895.
			4,560,000	3,250	76	January 10th, 1895.
11	30	F.	....	5,180	..	Tuberculous tube.
12	20	F.	5,936,000	5,400		
13	28	....	....	5,400		
14	44	M.	2,974,000	5,530	..	Pleuritic effusion also.
15	24	....	....	5,600		
16	34	...	....	5,600		
17	16	F.	3,840,000	6,000		
18	33	F.	4,000,000	6,000		
19	37	....	....	6,200		
				5,400		
20	3	....	6,008,000	6,200	45	
21	50	F.	5,240,000	6,400		
22	13	....	....	6,400	55	
23	37	M.	....	6,700	..	May 22d, 1896.
24	22	...	3,552,000	6,800	45	
25	30	M.	5,560,000	6,800		
26	15	...	5,112,000	6,900	70	Polynuclear, 44 per cent; lymphocytes, 49 per cent, eosinophiles, 7 per cent
27	44	F.	....	7,000	73	
28	19	....	....	7,200		
29	37	....	4,556,000	7,300	52	April 18th.

TABLE XXXVIII. (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
			4,616,000	....	56	April 25th.
			4,050,000	....	50	May 5th.
			3,880,000	....	52	May 10th.
			3,960,000	...	47	May 20th.
30	16	....	....	7,400	70	
31	15	...	....	7,400		
32	28	....	....	6,800		
33	26	M	4,368,000	7,400	45	
34	33	....	....	7,900		
35	31	...	....	8,000		
36	17	M.	4,904,000	8,000	75	
37	48	....	....	8,000	60	
38	33	F.	....	8,200		
39	20	F.	4,200,000	8,500	58	Tuberculous tube.
40	29	F.	3,400,000	8,600	80	
41	16	....	....	8,700	..	First day.
				7,600	..	Thirtieth day.
42	15	....	....	9,800		
43	19	...	.. ...	9,800		
44	50	F.	4,600,000	10,000	50	
45	41	M.	5,200,000	10,000		
46	20	....	.... ..	10,800		
47	38	F.	4,816,000	11,200		
48	47	....	.. ....	11,800		
49	21	F.	3,555,000	11,500	65	
50	19	....	....	11,600	65	
51	37	....	....	12,400		
52	5	....	4,472,000	14,200	50	
53	19	....	....	14,500		
				11,600		
54	15	....	....	14,600		
55	19	....	....	16,000	80	March 24th.
				14,000	..	March 26th.
56	16	....	....	16,100	..	First day.
				14,200	..	Sixth day.
				11,000	..	Eighth day.
57	27	F.	....	16,900	76	Pelvic abscess also.
				18,300		
58	6	....	4,576,000	18,000	52	Intestines perforated.
				31,900	..	Ninth day, after two dry taps.
				18,500	45	Thirteenth day, pus and fæces coming through tap holes.
				22,900	..	Seventy-eighth day. Autopsy.
59	11	...	....	18,200	60	
60	16	....	....	18,600	85	

I know of few differential counts of leucocytes in tuberculous peritonitis.

2. TUBERCULOUS MENINGITIS.

Remarkably few counts are on record so far as I can ascertain. Von Limbeck gives but a single case (with autopsy). Four counts, the last on the day of death, showed the following:

May 22d, 1889: Leucocytes	8,000
" 23d, 1889. "	8,000
" 24th, 1889. "	6,000
" 26th, 1889: "	7,500

Rieder records two cases, in one of which the leucocytes were "normal or subnormal, in the other increased." In both diagnosis was confirmed by autopsy. The counts in these cases were as follows:

Case I.—February 26th, 1891: Leucocytes	7,800
March 2d, 1891: Leucocytes	5,900
Case II.—May 30th, 1891: Leucocytes	14,400

Türck studied three cases, all showing more or less leucocytosis (9,600 with 90 per cent polynuclears and no eosinophiles, 17,100 and 18,100 with 83 per cent polynuclears and no eosinophiles, 20,800 with 86 per cent polynuclears and no eosinophiles). Blood plates and fibrin were *not* increased.

Pick saw two cases:

Case I.—February 28th, 1890: Leucocytes	6,500
March 5th, 1890: Leucocytes	8,000

In the second case there was also no leucocytosis. Autopsy in both. Sorensen's[1] two cases showed respectively 8,300 and 9,400 leucocytes. My own results in forty-three cases are as follows:

TABLE XXXIX.—TUBERCULOUS MENINGITIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	9 mos.	....	....	52,000	70	April 30th.
				31,000	...	May 3d.
						Death, May 5th.
2	2	....	....	29,900		
3	1	...	....	29,000	70	February 21st.
				51,000	....	February 26th. Autopsy.

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[1] Cited by Rieder.

TABLE XXXIX.—TUBERCULOUS MENINGITIS (*Continued*).

	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
4	2½	M.	....	28,000	63	July 8th.
				34,300	....	July 9th. Autopsy.
5	9 mos.	....	....	27,000		
6	2	F.	....	25,900	....	May 30th.
				23,800	....	June 4th. Tuberculous peritonitis also.
				32,800	...	June 8th.
				27,800	....	June 10th.
				23,600	....	June 12th.
				16,500	....	June 14th.
				21,000	....	June 16th.
				19,800	....	June 18th.
7	11	...	....	24,800	....	First day.
				32,700	....	Third day.
				32,600	....	Fifth day. Death.
8	5	....	....	24,000	....	August 28th.
				17,000	....	August 30th.
						Bronchopneumonia. Death.
9	9	....	....	22,400	80	Death.
	34	M.	....	21,500	....	Autopsy.
	8	....	....	20,400		
	0 mos.	....	....	19,500		
13	9 mos.	...	....	17,600		
14	10 mos.	....	....	16,400	....	Temperature 103° F., first day.
				29,500	....	Death, fifth day.
15	3	....	....	15,600		
16	3	....	....	15,400	55	
17	23	....	....	15,300	90	December 1st.
				20,000	....	December 3d.
				41,000	....	December 4th.
						December 5th. Death.
18	13	...	....	15,050	80	February 9th.
				20,500	....	February 21st.
				25,000	....	February 23d. Death.
19	35	M.	....	14,700	68	Pleurisy also.
20	22	M.	....	14,400	....	January 25th.
				19,400	....	January 30th.
				13,200	....	February 2d.
				19,300	...	February 6th. Autopsy.
21	6	....	....	14,000	....	First day.
				18,000	....	Fifth day.
22	6	....	....	13,900	....	First day.
				21,400	....	Fourth day, temperature 102° F.
				17,400	....	Tenth day.
23	46	....	... .	13,900	80	Death.
24	11	....	....	13,500	80	April 3d.
				11,800	....	April 18th.
				12,200	....	April 20th.
25	5	....	....	13,400	75	Death.
26	3	....	....	13,100		
27	23	....	....	12,200	95	November 5th.
				16,200	....	November 7th.

TABLE XXXIX.—TUBERCULOUS MENINGITIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
				16,700	....	November 10th.
				14,000	....	November 12th.
					....	November 18th. Death.
28	12	...	....	12,000		
29	8	....	....	11,500	....	First day
				11,900	....	Fourth day.
30	2¼	...	.. ....	11,000	65	Death.
31	35	..	....	10,800		
32	18	....	.. ....	10,500	80	Temperature 107° F. Death.
33	....	....	.. ....	10,000	....	First day.
				11,000	....	Fourth day.
34	10	....	....	9,400	90	Death.
35	10 mos.	....	....	9,200		
36	22	....	....	8,200	....	First day.
				13,300	....	Seventh day.
37	30	....	....	8,100		
38	45	M.	....	8,000		
39	5	....	....	7,500		
40	40	....	....	7,000	....	First day.
				10,000	...	Fourth day.
41	24	F.	4,590,000	6,600	86	
42	20	....	4,792,000	6,100	50	November 28th.
				6,200	....	November 30th.
				6,300	....	December 3d.
					....	December 6th. Death.
43	31	....	....	2,000	70	May 29th.
				3,200	....	May 31st.
				2,600	....	June 5th.
				29,300	....	June 10th.
						June 12th. Death.

In thirty-two of my forty-three cases there was leucocytosis, sometimes very marked.

Hoagland, of Colorado Springs, found in four cases the following:

Case.	Age.	No. of days before death.	White cells.	Per cent polynuclears.	Per cent lymphocytes.	Per cent eosinophiles.	Per cent myelocytes.
1	3	10	18,000	87	12.5	0.5	0.0
2	2	14	28,000	90	9.0	1.0	0 0
3	4	18	16,000	83	16.7	.3	0.0
4	3	12	29,000	82	17.0	.5	.5

The red cells and hæmoglobin show, as a rule, but slight changes, as is so often found in other forms of tuberculosis. The absence

ase in fibrin is, Türck thinks, of some diagnostic value
g other types of meningitis.

therefore that pure tuberculous meningitis differs mark-
ther pure tuberculous processes, in that it has a strong
y to raise the leucocyte count. Osler's results point to the
nclusion.[1] Ziemke[2] has recently reported a case with 17,500
s per cubic millimetre.

3. Tuberculous Pericarditis.

case in which tubercle bacilli were repeatedly demon-
in the fluid obtained by tapping the pericardial sac I found
cocytosis. The counts in two others are shown in the accom-
ing table. I have not met with any other reports on the blood
s condition.

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	..	....	6,200		
	..	4,728,000	7,000	60	

4. Tuberculous Pleurisy.

No doubt a large proportion of all pleuritic effusions are tuberculous in origin; and, so far as I have seen, no high counts are recorded in cases proved by culture or inoculation to be tuberculous. The low leucocyte counts in most pleurisies (see page 276) tend to show that they are tuberculous and not due to pyogenic organisms.

Pick mentions that he finds no leucocytosis in tuberculous pleurisy when uncomplicated by phthisis, but reports no actual counts.

5. Glandular Tuberculosis.

In cases of so-called scrofulous glands, whether in children or adults, the blood shows no important changes except that in children the hæmoglobin may be considerably diminished.

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[1] "Text-book of Medicine," 3d edition.

[2] Deut. med. Woch., April 8th, 1897.

GLANDULAR TUBERCULOSIS.

No.	Age.	Sex.	White cells.	Per cent hæmoglobin.
1	20	F.	5,600	75
2	28	M.	10,900	65
3	7	F.	11,000	

Leucocytosis is absent unless an abscess has been opened and infected. Whether or not tuberculosis of the abdominal or other internal lymph glands affects the blood, I am unable to say.

6. GENITO-URINARY TUBERCULOSIS.

Here the opportunities for a secondary pyogenic infection are so good that in about one-fourth of the cases we find the blood of septicæmia present. The following cases, all involving the bladder, kidney, and the external genitals, illustrate this point:

TABLE XL.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	40	....	....	29,200	65	December 9th, Ren mobilis; tuberculous laryngitis.
				20,800	..	December 10th.
				20,200	..	December 15th.
2	65	....	....	21,800	65	August 6th.
				25,600	..	August 10th.
				29,600	..	August 11th.
				42,400	..	August 13th.
				38,000	..	August 17th.
				25,600	..	August 19th.
				23,600	..	August 21st.
				28,000	..	August 24th.
				26,600	..	August 28th, death.
3	50	....	....	20,100	58	
4	23	....	....	15,100		
5	6	....	....	15,000	62	T. B. in urine; kidney operated.
6	30	M.	3,796,000	14,452	44	
7	23	....	....	12,600	..	Bladder.
8	31	....	....	11,000	55	Kidney.
9	40	....	....	10,400	50	
10	41	F.	3,588,000	10,400		
			3,000,000+	14,452		
11	26	..	4,564,000	10,400	40	T B. of right kidney with pleurisy. March 18th.
			3,532,000	11,300	40	March 25th.
			3,632,000	.. ..	38	April 9th.

TABLE XL. (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
			3,320,000	11,300	40	April 16th, differential count: Polynuclear, 87.8 per cent; small lymphocytes, 7.4 per cent; large lymphocytes, 3.6 per cent; eosinophiles, 1.2 per cent.
			3,624,000	7,500	43	April 27th.
			3,492,000	......	35	May 11th.
			3,712,000	......	43	May 19th.
			3,936,000	......	47	May 28th.
12	22	F.	....	10,200		
13	27	....	....	10,100		
14	56	....	... .	10,100	..	Testicle and lung.
15	32	....	....	9,700		
16	9	....	....	9,400	70	
17	64	....	....	9,300		
18	33	....	....	9,000	..	Kidney. Death.
19	35	F.	5,808,000	8,800	65	
20	8	....	....	8,500	70	
21	22	F.	....	8,400		
22	43	....	....	7,800	80	
23	42	...	....	7,600	90	
24	31	M.	....	7,600	57	
25	27	...	....	7,400	100	
26	31	F.	....	6,900	60	
27	42	M.	....	7,000	..	December 18th.
				8,700	..	December 26th.
				8,300	..	January 11th.

SYPHILIS.

Reiss, in an article in the *Archiv f. Dermatologie und Syphilis*, 1895, Heft 1, says that the general constitutional influence of the poison of syphilis is best indicated by the condition of the blood. In one hundred cases he has arrived at the following conclusions regarding the

Red Cells and Hæmoglobin.

During the time between the chancre and the secondary symptoms, the red cells are slightly decreased, but this is much more marked after the appearance of secondary symptoms and continues for a time even after treatment has begun. The hæmoglobin sinks steadily from the time of the primary lesion on, but is not especially affected by the eruption. Even under treatment the hæmoglobin *never* gets quite up to normal and prolonged mercurial treatment lowers it, although mercury has at first a beneficial effect on the hæmoglobin as well as on the other constituents of the blood.

Konried[1] goes further into detail. According to him, in the first four to seven weeks after infection, the number of red cells remains normal, but the hæmoglobin begins to fall off, losing from ten to twenty per cent in that time. Afterward it sinks steadily until treatment is begun, the number of corpuscles also falling slightly.

Newmann and Konried[2] reporting in 1893 on two hundred cases, say that up to the time of the secondary symptoms from twenty-five to thirty per cent of hæmoglobin is generally lost, without much change in the red cells, which sink considerably in number after the outbreak of secondary lesions. Lezius[3] likewise finds no diminution in the *number* of red cells until the outbreak of secondary lesions.

Ewing says: "With the outbreak of secondary symptoms the red cells begin to fall rapidly, reaching in untreated cases as low as 2,000,000 or less (Konried). In ten cases Wilbouchewitch found an average decrease of 229,000 cells daily. At the same time the hæmoglobin continues to diminish and may fall to 55–25 per cent within a few weeks or months."

All these changes, like those about to be described, are apt to be more marked in women than in men. In cases going on to the secondary stage untreated, the hæmoglobin may sink to as low as twenty-five per cent. In the tertiary stages and in hereditary and so-called "constitutional syphilis" the red corpuscles are much more seriously affected, diminishing considerably in number as well as in weight and color. The hereditary syphilis of infancy may indeed produce fatal anæmia and very low counts are common, with large numbers of nucleated red cells and great deformities in shape and size.

The effect of mercurial treatment on the red cells is interesting. Gaillard[4] found that the count of red cells increased during the first fourteen days, and the hæmoglobin during the first twenty-four days of treatment. After that time, if mercury was still given, the hæmoglobin and later the number of corpuscles began to decline.

Konried (*loc. cit.*) found the hæmoglobin to rise during the administration of the first twenty-five to thirty-five innunctions, after which it began to go down. This was in cases in which treatment was begun just after the onset of secondary symptoms. In the worst cases it sank even as low as forty-five per cent despite treatment, and this usually means a bad prognosis and severe tertiary symptoms to come. In one of my own cases the hæmoglobin was only thirty-seven per cent, though the red cells were 4,988,000 (color index, 0.37).

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[1] International Dermatological Congress, 1892.

[2] Wiener klin. Woch., 1893, No. 19.

[3] Inaug.-Dissert., Dorpat, 1889.

[4] Gaz. des Hôp., 1885, No. 74.

Ewing says: "In one the spleen was much enlarged and contained gummata, while the blood showed the lesion of grave secondary anæmia, with a tendency toward the microcytic type and a low hæmoglobin index. In other cases the abundant megalocytes with increased hæmoglobin closely resembled those of pernicious anæmia."

Potassic iodide increases the red cells and hæmoglobin, but has no special effect on the leucocytes.

Cases often show spontaneous improvement in their anæmia as well as in other symptoms.

Justus[1] in five hundred cases claims to have observed, in seventy to eighty per cent of all cases of syphilis, a peculiar reaction of the hæmoglobin, which does not occur in any other disease and which he considers of much diagnostic value.

According to him, if in cases in which secondary symptoms have not yet appeared, we test the hæmoglobin and then give an inunction or a subcutaneous injection of mercury, we find that within twenty-four hours a very marked fall in hæmoglobin has taken place (ten to twenty per cent), owing to the action of the mercury on the weakened corpuscles. This sudden fall is followed by a gradual rise until within a few days the coloring matter is at a point slightly higher than before the mercury was given. In diseases other than syphilis this sudden drop does not occur. After the advent of secondary symptoms the peculiar reaction to mercury does not occur. My own experience with the test is small. In nine cases of active syphilis I found it present. In three inactive cases and in thirty-five control cases of various other diseases it was absent. In a case of chlorosis the reaction was positive.

Brown and Dale[2] studied thirteen cases of syphilis, and concluded that the test is unreliable and of little practical value. In some of their cases the drop in hæmoglobin did not appear until several inunctions had been given.

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[1] Justus: Deut. Arch. f. klin. Med., vol. 75.

[2] Cincinnati Lancet-Clinic, March 24th, 1900.

Jones[1] examined thirty-five syphilitics and eighteen control cases. Of seventeen cases of active syphilis thirteen gave positive results. Jones thinks the test of some value in diagnosis though by no means pathognomonic.

Christian and Foerster (*University Medical Magazine*, November, 1900) studied twenty-nine cases and found the test quite unreliable. They obtained positive reactions in neurasthenia and two cases of chancroid. On the whole I agree with their conclusions.

White Cells.

1. Here the changes are not characteristic. In the first stage the leucocytes are either normal or slightly increased, but the percentage of polymorphonuclear forms is almost always notably low and that of the lymphocytes high. If mercury is given at this stage, the polymorphonuclear forms begin to increase toward normal, and the lymphocytes proportionately to decrease. [Mercury given to healthy persons has just the opposite effect, increasing the lymphocytes at the expense of the polymorphonuclear forms.] Iodide of potassium works exactly like mercury in this respect, increasing the polymorphonuclear leucocytes in syphilis, while it diminishes them in healthy persons.

2. As the eruption breaks out leucocytosis (12,750 and 16,800 in two of my cases) sometimes appears, the proportion of lymphocytes usually being increased. Various writers have reported an eosinophilia at one or another stage of the disease, but Peter,[2] who has carefully studied this point, states that eosinophilia is never produced by syphilis at any stage, though from various causes the eosinophiles may be temporarily increased. Engel describes a syphilitic child in whom the percentage of polymorphonuclear cells steadily rose as the child got worse. In such cases Engel considers these cells to be of prognostic importance. P. K. Brown has made a similar observation in bone tuberculosis. Treatment with mercury and potassium iodide tends to bring down the count of lymphocytes, and to increase the polymorphonuclear forms, while it raises the count of red cells.

In the *tertiary stages*, with the severe anæmia which is often present, there occur occasionally leucocytosis, not uncommonly with small percentages of myelocytes, and a marked lymphocytosis. Müller[1] has described four cases of anæmia in syphilis so severe as to simulate pernicious anæmia very closely. In one the red cells sank to 720,000. Laache[2] mentions a similar case.

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[1] New York Med. Jour., April 7th, 1900.

[2] Peter: Dermat. Zeit., 1897, vol. iv., p. 669.

There are no constant changes in the blood plates. They are often increased in anæmic cases and are in all probability the bodies described by Losdorfer as specific and characteristic of syphilis. (See discussion by Vörner.[3]) The specific gravity follows pretty closely the hæmoglobin percentage.

Diagnostic Value.

Justus' reaction of syphilitic blood to mercury, if true, would be of great value in distinguishing early syphilis from various other causes of debility, but it is in all probability useless.

The chief value of the blood examination in syphilis is not for diagnosis but as a measure of the stage and severity of the infection. Low hæmoglobin and high percentages of the lymphocytes are characteristic of severe types. Leucocytosis usually means that the case has got beyond the primary stage, while in the tertiary stage the presence of myelocytes with a marked anæmia is of serious import.

Certain cases of this last type may closely resemble pernicious anæmia, from which, however, they are to be distinguished by their low color index, the frequent presence of leucocytosis, and the relative infrequency of megaloblasts as compared with the normoblasts, in case nucleated red cells are present.

TABLE XLI.—SYPHILIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	. .	....	....	24,000	70	Meningitis.
2	30	....	... .	24,000	90	Cerebral.
3	31	....	....	18,600	...	Tertiary. Liver?
4	27	....	....	16,500	...	Hemiplegia.
				12,700	...	Eleventh day.
5	25	....	....	15,900	80	Cerebral.
6	11	....	....	15,200	75	Cerebral. June 4th.
				15,130	...	June 8th.

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[1] Charité-Annalen, vol. xiv.

[2] *Loc. cit.*

[3] Vörner: Deut. med. Woch., December 11th, 1902.

TABLE XLI.—SYPHILIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
				13,400	...	June 14th.
				14,260	...	June 21st.
7	30	...	....	15,000	...	Temperature 100°, with iritis.
8	45	....	....	14,800	...	Cerebral.
9	11	....	....	14,400	72	Cerebral.
10	23	...	....	14,200	80	
11	40	...	... .	13,200	...	Cerebral.
12	59	....	....	12,600	88	Cerebral.
13	31	....	....	12,100	70	Secondary.
14	24	....	....	11,300	80	Cerebral.
15	36	....	....	10,350	65	Cerebral.
16	48	....	....	9,700	...	Cerebral.
17	53	....	....	9,400	100	Cerebral.
18	29	....	5,880,000	8,640	52	Amyloid liver and spleen.
19	33	....	....	8,600		
20	51	....	....	8,400	100	Liver.
21	66	....	....	7,960	81	Cerebral.
22	28	....	....	7,600	65	Tertiary.
23	31	....	....	7,200		
24	35	..	5,280,000	6,900	55	Myocarditis; larynx.
25	40	....	....	6,600	70	Cerebral.
26	49	....	....	6,500		
27	38	....	....	6,000	65	
28	70	....	....	6,000	85	Tertiary.
29	24	....	....	5,600	70	
30	32	....	....	4,500	...	Testicle.

Dr. Thomas J. Yarrow kindly sends me a blood report of the following case, apparently of hereditary syphilis:

	Dec. 12th, 1898.	Dec. 20th.	Jan. 4th, 1899.	Jan. 27th.	Remarks.
Red cells.......	3,350,000				
White cells.....	20,000				
Polynuclear....	35.0%	26.7%	39.8%	52.8%	The blood changes here reported coincided with the use of mercury and with the disappearance of the anæmia and of all symptoms.
Lymphocytes...	44.6%	54.4%	52. %	43.8%	
Eosinophiles....	20.6%	18.7%	8. %	3.4%	
Normoblasts....	60 per c.mm.				

LEPROSY.

Winiarski (*Petersburger medicinische Wochenschrift*, 1892, p. 365) gives a careful study of seventeen cases of leprosy, and P. K.

watched sixteen cases. They find in young persons
ises no changes from the normal blood.
e cases, especially in old people, the anæmia may be
0,000 red cells with 54 per cent of hæmoglobin) and
arable to pernicious anæmia (1,989,000 red cells with
t of hæmoglobin). In anæmic cases the color index is
igh, in one case it was 1.7 (!). Such severe types
ociated with an increase of the average diameter of the red
which explains the high color index. The hæmoglobin was
vely low in any case.

Leucocytes.

o increase was present in any case. Four cases were subnor-
The percentage of lymphocytes, as in other debilitated con-
, is often high (forty-five to forty-seven per cent). Eosino-
has been recently noticed by Bensaude,[2] by Achard and
r[3] (five to eleven per cent), and by Sabrazès and Mathes,[4] the
only in nodular cases and not in those of the anæsthetic type.

Bacteriology of the Blood.

Brown has succeeded in demonstrating the leprosy bacillus in the blood of one-half of his cases. The bacilli appear for the most part within the leucocytes, and here they accumulate in large numbers. It is especially in the tubercular form of the disease that Brown has found them. He was unable to cultivate the bacillus.

Streker[5] has likewise found the bacillus in the blood of four cases.

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[1] San Francisco County Medical Society, July 13th, 1897.

[2] Bensaude: Ref. in Presse méd., 1898, p. 806.

[3] Achard and Loeper: Ref. in Brown's article in Internat. Clinics, vol. iv., 12th series.

[4] Sabrazès et Mathes: Gaz. Hebd., 1902, No. 2.

[5] Streker: Münch. med. Woch., 1897, Nos. 39 and 40.

PART IV.

DISEASES OF SPECIAL ORGANS.

CHAPTER VII.

DISEASES OF THE DIGESTIVE APPARATUS.

1. MOUTH.

In a case of thrush complicating chronic nephritis the following counts were recently recorded at the Massachusetss General Hospital: October 16th—red cells, 5,000,000; white cells, 16,200; hæmoglobin, 52 per cent. October 24th—white cells, 13,800; hæmoglobin, 55 per cent.

2. Œsophagus (see Malignant Disease, page 439).

3. Stomach. Displacements of the organ (gastroptosis) have no effect upon the blood.

The conditions existing in the stomach may influence the blood profoundly in three ways:

(*a*) They may be such as to prevent the normal absorption of nitrogenous material on which the blood, like all tissues, is absolutely dependent. Then the blood becomes starved. The extreme of this condition is the so-called "atrophy of the gastric tubules," which may produce fatal anæmia. In lesser degrees the same process is at work in many forms of chronic dyspepsia, gastritis, or chronic starvation.

(*b*) They may lead to severe and repeated hemorrhages.

(*c*) They may lead to an auto-intoxication which poisons the blood as well as other tissues.

On the other hand, it is probably through the influence of an altered blood serum on the duodenal mucous membranes that ulcer of the duodenum is a sequel to severe burns of the surface of the body.

For an account of the influence on the blood of digestion, ingestion of liquid, and starvation, see page 90.

DISEASES OF THE STOMACH.

ANOREXIA NERVOSA.

From pure starvation the red cells may get as low as 900,000, as in the case mentioned by Martin. In the early stages the blood is normal A recent hospital case showed 8,900 leucocytes with 87 per cent of hæmoglobin.

GASTRIC CANCER.

(See Malignant Disease, page 433.)

GASTRIC ULCER.

Red Cells and Hæmoglobin.

A severe anæmia is common. Out of the 51 cases in Table XLII., A, 42—80 per cent—had less than 50 per cent of hæmoglobin, and of the 51 in which the red cells were counted, 17 had under 3,000,000 red cells per cubic millimetre. The average count of red cells at the time when treatment began was 3,372,000. There is no single disease, so far as I am aware, in which the red cells are so apt to be so low, except pernicious anæmia. Even cancer, as a rule, does not fall so low. This is due mostly, I think, to the frequency of *hemorrhage* from the ulcer; it is uncommon to see marked anæmia in patients who have never had a hemorrhage.

This anæmia is all the more striking when we remember that the frequent vomiting from which most patients suffer tends to concentrate the blood, *increase* the number of cells in a drop, and so to make the blood seem less anæmic than it really is. This tendency to concentration is probably effective in some of the cases observed especially by Oppenheimer,[1] in which despite great pallor he found normal counts of red cells and hæmoglobin.

It is in such cases that the estimation of the dry residue of the blood serum would be of real value could it be made short and simple enough for clinical work Grawitz, who is the prophet of this branch of blood examination, gives an interesting case illustrating this point.

A girl of twenty-five, suffering with peptic ulcer, and exceedingly pale, showed, on counting the corpuscles, 4,140,000 per cubic millimetre (no considerable reduction), and 90 per cent of hæmoglobin. A second count showed

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[1] Deut. med. Woch., 1889, No. 42.

4,340,000 corpuscles and 91 per cent of hæmoglobin. But the dry residue of the serum was reduced to three-fourths its normal amount. The serum suffers in anæmia as much as the corpuscles do. Any influence which deprived the serum of one-fourth of its normal solids (œdema being absent) must have really affected the corpuscles very much. Therefore the corpuscles must actually have been reduced to about 3,800,000, the reduction being masked by the concentration of the blood from vomiting. Lymph cannot have run into the vessels and diluted the serum, for (owing to the vomiting) the tide is all the other way. If then the serum is reduced to a quarter the corpuscles must be so likewise. Unfortunately, to test the dry residue of the blood serum requires more time, skill, and apparatus than clinicians are apt to have. It is valuable whenever we wish to know whether or not an anæmia is being masked by concentration of the blood.

In severe cases the usual *qualitative evidences* of secondary anæmia (deformities, scanty normoblasts) are to be found.

TABLE XLII., A.—GASTRIC ULCER WITH HEMORRHAGE.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	32	..	4,864,000	22,000	75	Hemorrhage yesterday.
2	20	..	3,968,000	21,100	45	Chlorosis.
3	52	F.	2,031,000	17,200	30	Hemorrhage and perforation.
4	27	..	1,860,000	15,300	20	Vomited small amount of blood.
5	23	..	3,480,000	15,000	43	
6	35	M.	1,640,000	14,900	18	Bled four days ago. Diff. count 500 cells: Polynuclear, 74 per cent. Lymphocytes, 25 " Eosinophiles, .4 " Myelocytes, .6 " Megaloblasts, 4 Normoblasts, 1 Reds stain well. Many polychromatophilic.
			2,104,000	6,100	24	Sixth day. Diff. count 500 cells: Polynuclear, 60 per cent. Lymphocytes, 39 " Eosinophiles, 1 " Megaloblasts, 0 Normoblasts, 1
			2,566,006	7,000	32	Thirteenth day. Diff. count 500 cells: Polynuclear, 58 per cent. Lymphocytes 39 " Eosinophiles, 3 " No nucleated reds.
			3,192,000	....	40	Twenty-first day.
			4,008,000	6.600	55	Thirty-second day.
7	29	F.	1,676,000	14,750	36	Large hemorrhage.
8	55	F.	3,664,000	14,800	45	
9	22	..	4,820,000	13,800	50	Perforation.

TABLE XLII. A.—GASTRIC ULCER WITH HEMORRHAGE (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
10	48	..	1,448,000	13,700	10	Five days after perforation. Diff. count 500 cells: Polynuclear, 86 per cent. Lymphocytes, 13.6 " Eosinophiles, .4 " Normoblasts, 1
11	42	F.	2,216,000	13,500	32	
12	32	..	3,256,000	13,000	35	November 11th.
			2,564,000	?	20	November 14th. Polynuclear, 83.2 per cent. S. lymphocytes, 10.4 " L. lymphocytes, 3.6 " Eosinophiles, 1.8 " Myelocytes, 1 " No nucleated reds; general tendency to small size, very few large forms: moderate poikilocytosis.
13	24	..	5,016,000	12,000	52	
14	29	..	3,644,000	11,400	35	Day after hemorrhage of O iij.
15	72	..	3,799,000	10,700	35	Autopsy.
16	35	..	3,024,000	10,200	55	January 2d.
			3,392,000	?	55	January 13th.
			3,712,000	....	45	February 5th.
17	40	..	3,868,000	9,900	50	
18	17	..	5,000,000	9,700	45	
19	27	..	4,092,000	9,300	40	
20	35	..	1,364,000	17,200	20	No autopsy.
			2,224,000	9,200	40	
21	24	F.	3,076,000	8,900	15	Bleeding.
22	20	..	5,374,000	8,650	65	
23	37	..	3,267,000	8,500	30	Hemorrhage six days ago.
24	45	..	3,520,000	8,400	35	
25	37	..	4,188,000	8,100	35	Bled one month ago.
26	30	F.	3,432,000	7,820	45	Hemorrhage previous day.
			4,222,000	10,600	75	Two weeks later.
			4,392,000	6,700	70	Three weeks later.
27	44	..	4,020,000	7,600	33	
28	29	..	5,000,000	7,400	50	Slight hemorrhage.
29	26	..	1,888,000	7,400	19	Three days after hemorrhage: Polynuclear, 57 per cent. Lymphocytes, 41 " Eosinophiles, 2 " No nucleated reds; reds small but not much deformed.
30	22	..	2,984,000	7,200	..	October 3d.
			3,436,000	?	21	October 20th.
			3,612,000	?	34	November 1st.
31	24	F.	1,892,000	7,000	30	January 16th, after hemorrhage.
			2,304,000	?	27	January 22d.
			3,064,000	3,500	35	January 31st.
			3,920,000	?	48	February 10th.
			4,680,000	?	55	February 28th.
32	20	..	3,340,000	7,000	45	

TABLE XLII. A.—GASTRIC ULCER WITH HEMORRHAGE (*Continued.*)

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
33	52	..	1,712,000	7,000	25	Five days after hemorrhage. Diff. count 300 cells: Polynuclear, 64 per cent. Lymphocytes, 35 " Eosinophiles, 1 " Normoblasts, 1.
34	33	..	4,800,000	7,000	40	
35	26	..	3,280,000	6,800	30	
36	24	..	4,704,000	6,500	45	
37	30	..	2,544,000	6,400	30	
38	13	..	4,496,000	6,300	50	
39	48	F.	4,900,000	6,200	40	
40	23	F.	1,672,000	6,000	40	One pint of blood vomited yesterday; blood in stools; recovery.
41	30	..	3,920,000	6,000	30	Bled seven days ago.
42	24	..	3,196,000	5,900	15	
43	26	F.	2,968,000	5,300	45	Exclusive rectal feeding eight days.
44	19	..	4,432,000	5,000	58	Grippe and tonsillitis.
45	24	..	4,625,000	5,000	45	
46	50	M.	1,554,000	4,800	25	Polynuclear, 74 per cent. Lymphocytes, 23 " Eosinophiles, 2 " Normoblasts, 2.
47	46	M.	3,324,000	4,800	35	Fell to 15 per cent after hemorrhage.
48	29	..	2,584,000	4,500	25	
49	38	..	3,616,000	4,300	35	Eleven days after profuse hemorrhage.
50	29	F.	1,972,000	4,000	38	Recovery.
51	26	..	4,312,000	2,600	45	

GASTRIC ULCER WITH HEMORRHAGE.

White Cells.	Cases.
Between 2,000 and 6,000	17
" 6,000 " 8,000	23
" 8,000 " 10,000	17
" 10,000 " 12,000	6
" 12,000 " 14,000	10
" 14,000 " 16,000	7
" 16,000 " 20,000	3
" 20,000 " 24,000	3
Total	86

XLII., B.—Gastric Ulcer without Hemorrhage.

	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	27	....	....	22,000	90	October 31st.
				15,200	..	November 1st.
		....	5,716,000	13,600	85	
		....	....	12,800	60	March 14th; lead in urine
				6,800	65	March 20th.
				8,200	65	April 2d.
	17	....	5,380,000	12,100	60	
	22	....	5,040,000	12,000	45	
	25	....	....	11,900	80	July 20th.
					70	July 30th.
				13,600	80	August 8th.
	21	....	5,000,000	11,800	70	
	39	F.	....	11,100	68	
	51	....	....	10,800	70	
	24	....	6,988,000	10,700	48	Vomiting.
	19	F.	5,856,000	10,650	90	
	22	...	....	19,200	85	
		F.	4,400,000	9,000	53	
		F.	....	9,300	90	
	22	F.	....	8,300	75	
	29	....	....	8,100	65	
	27	....	....	7,000	75	
	30	....	....	6,800	70	
	30	....	....	6,800	70	
				3,400	...	Before test breakfast.
				3,500	..	After test breakfast.
20	30	F.	....	6,800	70	
21	25	....	....	6,550	85	
22	35	....	....	6,500	50	April 27th.
					45	June 6th.
23	47	F.	....	6,300	57	
24	21	....	....	6,000	90	
25	38	F.	....	5,800	60	
26	19	F.	....	5,600	68	
27	20	F.	....	4,300	57	
28	26	....	3,216,000	4,200	30	
29	23	....	4,680,000	....	25	
30	21	F.	5,100,000	....	70	

Hæmoglobin.

As a rule the color index is low. Only one examination in the cases of the Massachusetts General Hospital series showed an increased amount of hæmoglobin per corpuscle, and as this was not repeated or verified, it may have been a mistake. In most of the other examinations the color index was low.

Yet Osterspey records 1,900,000 red cells with 31 per cent of hæmoglobin (color index = .81); 3,296,000 with 70-per-cent hæmoglobin (color index = 1.09); 4,048,000 with 84-per-cent hæmoglobin (color index = 1.05). Such cases are certainly rare.

White Cells.

Leucocytosis is practically never seen except after hemorrhage and during digestion. When patients who have been fed for some time by the rectum are first given food by the mouth, the digestion leucocytosis may be very great, as in a case of the above series, in which the cells increased from 4,000 to 15,500! The presence of a leucocytosis, when the influence of bleeding and digestion is excluded, is against the diagnosis of ulcer of the stomach.

TABLE XLIII.—DUODENAL ULCER

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	53	..	1,472,000	24,000	20	September 3d. Diff. count 500 cells: Polynuclear, 75 per cent; small lymphocytes, 22.4; large lymphocytes, 1.2; eosinophiles, 1.2; myelocytes, 0.2; one normoblast.
			1,876,000	... ...	19	September 10th.
			2,148,000	....	17	September 18th.
			2,440,000	....	21	September 24th.
			3,196,000	... .	23	October 1st.
			2,904,000	6,600	28	October 8th.
			2,744,000	....	23	October 16th.
			2,820,000	....	30	October 23d.
					39	October 30th.
			3,440,000	....	43	November 6th.
			3,832,000	....	45	November 24th.
			3,885,000	....	48	December 15th.
2	31	..	1,960,000	24,000	28	October 27. Diff. count: Polynuclear, 86 per cent; small lymphocytes, 10; large lymphocytes, 1.2; eosinophiles, 2; normoblasts, 1.
			1,764,000	10,500	25	October 31st.
			3,232,000	24,000	40	November 6th.
				17,200	45	November 8th.
			3,104,000	8,000	45	November 14th.
			3,968,000	....	48	November 22d.
			3,520,000	....	50	November 26th.
3	38	..	....	15,800	80	July 11th.
			5,296,000	14,800	75	July 16th.
			1,448,000	9,700		
				14,200	..	July 23d.
				18,300	..	July 27th.
				14,800	..	July 29th.
			1,928,000	7,800	10	August 2d. Diff. count 200 cells: Polynuclear, 65.5 per cent; small lymphocytes, 25.5; large lymphocytes, 9; eosinophiles, 0; megaloblasts, 1; normoblasts, 4.

TABLE XLIII.—DUODENAL ULCER (*Continued*).

.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
						August 8th Diff. count 200 cells: Polynuclear, 70 per cent; small lymphocytes, 13; large lymphocytes, 16.5; eosinophiles, 0.5; normoblasts, 4.
			1,976,000	......	15	August 14th.
			2,500,000	13,800	15	August 20th Diff count 200 cells: Polynuclear, 72.5 per cent; small lymphocytes, 14; large lymphocytes, 13; eosinophiles, 5.
			2,476,000	10,800	25	August 26th.
			2,840,000	12,500	25	September 2d.
			2,746,000	10,800	25	September 9th.
4	47	M	2,100,000	12,000	35	July 24th, much coffee grounds.
				7,650	..	July 29th (five days fasting).
				11,600	..	Four hours after meal.
				11,000	..	Constant feeding, July 30th.
			2,480,000	6,000	38	August 8th.
			2,630,000	6,500	36	August 21st, operation.
	54	..	2,016,000	11,600	45	Death.
	29	..	....	10,800	80	
7	48	..	....	9,200	88	
8	35	..	....	7,900	53	
9	50	.	....	7,800	62	
10	30	..	3,776,000	Normal.	50	
11	38	..	1,700,000	Normal.	67	
12	47	..	2,584,000	5,600	35	August 7th.
			996,000	8,000	15	August 8th, death.

These figures are given simply to show that the blood in duodenal ulcer undergoes much the same changes as in gastric ulcer, and needs no further comment.

ACUTE GASTRITIS AND DYSPEPSIA.

Acute gastritis or gastro-enteric attacks (Hayem's "*embarras gastrique*") do not affect the red cells or hæmoglobin, but are very often accompanied by leucocytosis (see Tables XLIV., A and B).

TABLE XLIV., A.—ACUTE GASTRO-ENTERITIS

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	2	..	......	19,700	75	September 23d, temp. 102°.
				13,800	.	September 27th.
2	72	.	....	19,400	90	May 22d, acute.
				30,400	..	May 26th.
				20,200	..	May 27th.

TABLE XLIV., A.—ACUTE GASTRO-ENTERITIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells	Per cent hæmo-globin.	Remarks.
				12,800	..	May 29th.
				9,200	..	June 5th.
3	31	M.	7,000,000	18,000	..	Temp. 104°. Well next day.
4	8	F.	4,800,000	17,800	50	Temp. 101°.
5	50	F.	....	15,100	70	
6	13	F.	5,184,000	15,000	85	Well next day.
7	28	M.	....	14,400	..	September 17th, temp. 103°.
				12,800	..	September 18th.
				9,100	..	September 21st, temp. normal.
8	30	F.	4,860,000	14,200	80	Well in three days.
9	20	M.	....	12,000	67	
10	36	F.	....	11,600	68	
11	23	F.	6,244,000	11,600	86	Well in two days.
12	..	..	....	11,500	..	August 5th.
				17,000	..	August 5th, 8 P.M.
				8,000	..	August 6th.
13	17	F.	4,600,000	11,000	70	
14	29	F.	....	11,000	..	Temp. 101°.
15	70	F.	4,632,000	10,000	90	
16	37	M.	4,186,000	9,200	68	
17	28	M.	....	6,900	90	Temp. 102°.
18	23	F.	3,860,000	6,400	65	
19	57	F.	....	6,000	..	Temp. 101°.
20	23	F.	5,144,000	5,400	95	
21	32	F.	....	5,200	50	Temp. 100°.

Where this is the case, it may help us to exclude typhoid fever, which has no leucocytosis. Even a twenty-four hours' dyspeptic attack may increase the leucocytes notably, as in Cases 1 and 2 in Table XLIV., A, and the presence of such an increase need not make us suspect anything behind the dyspepsia. It is probably to be classed as a toxic leucocytosis due to absorption of morbid products from stomach or intestine. Fibrin may be increased during the period of leucocytosis.

TABLE XLIV., B.—DYSPEPSIA AND GASTRITIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
1	24	M.	6,280,000	22,700	..	Gastralgia; constipation; whole belly tender.
				12,800	..	Three days later; well in a week.
2	22	..	....	21,000	90	Nervous periodic vomiting.
3	27	F.	4,750,000	14,000	74	At mealtime, 11,200; four hours later, 12,150.
4	26	F.	4,920,000	11,000	55	Dyspepsia.
5	23	M.	....	11,000	..	Acute gastritis.

TABLE XLIV., B.—DYSPEPSIA AND GASTRITIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
6	..	..	5,016,000	8,924	86	
7	37	M.	....	7,326	77	Chronic gastric catarrh.
8	30	F.	3,678,000	7,000	75	Nervous dyspepsia.
9	41	M.	4,524,000	6,000	68	Before meal, November 1st, 6,000; November 2d, 6,300. After meal, November 1st, 6,800; November 2d, 7,400.
10	49	F.	4,200,000	4,000	80	Chronic gastritis.
11	18	F.	5,016,000	3,200	45	Dyspepsia.
12	60	M.	3,504,000	2,800	50	Chronic gastritis.

CHRONIC GASTRITIS.

(See Cases 7, 10, and 12, Table XLIV., B.)

Here the conditions are different and we never find an increase of the white cells, but often a decrease to malnutrition. Digestion may produce no leucocytosis, or the increase may be very slight and late in appearing (four to five hours after a meal instead of two to three hours). It was present in nine out of twelve cases in our series.

Anæmia is very often present and may be extreme. It is believed by very high authorities that a *pernicious* anæmia may be caused by chronic gastritis with atrophy of the gastric tubules. The writer has never had the good fortune to see such cases.

The practical points about the blood of chronic gastritis are:

(*a*) The not infrequently severe anæmia.

(*b*) The not infrequent absence of digestion leucocytosis as in gastric cancer, from which therefore the *absence* of digestion leucocytosis does not distinguish it.

The presence of a leucocytosis militates against the diagnosis of chronic gastric catarrh, and, if hemorrhage is excluded, points toward cancer.

HYPERACIDITY AND HYPERSECRETION.

Lichty[1] found normal number of red cells and normal hæmoglobin in hyperchlorhydria, 39 cases; hypochlorhydria, 63; achylia gastrica, 6; gastric dilatation, 11; chronic gastritis, 13; nervous dyspepsia, 14.

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[1] Lichty: Phil. Med. Journ., 1899, p 326.

The leucocytes average higher in these conditions than in chronic gastritis or dyspepsia with normal or decreased secretions (see Table XLV.). Otherwise the blood is not remarkable.

TABLE XLV.—HYPERACIDITY AND HYPERSECRETION.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	55	..	....	14,000	75	
2	Adult.	M.	5,024,000	12,800	82	
3	80	F.	5,768,000	10,800	82	Chronic gastritis.
4	40	M.	5,800,000	10,000	85	Slight digestion leucocytosis; 12,270 before meal, 14.800 three hours later.
5	81	..	....	9,800	80	November 3d.
					85	November 11th.
6	58	..	....	8,700	72	
7	40	M.	8,840,000	7,780	72	Dilated stomach; no digestion leucocytosis.
8	27	..	4,848,000	7,400	60	Anæmia
9	87	..	... .	7,000	70	
10	60	..	....	6,600	85	
11	28	F	4,016,000	5,994	76	
12	57	M	4,160,000	3,600	84	Lead poisoning and dilated stomach

DILATED STOMACH

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	30	..	....	11,000	70	
2	22	..	6,216,000	10,400	83	
3	24	..	....	9,900	90	
4	29	..	....	9,600	78	Movable kidney
5	51	..	4,184,000	9,600		
6	47	..	4.720,000	8,000		
7	50	..	....	6,400	65	Before test breakfast, 10,200. After test breakfast, 5,500.
8	30	..	5,000,000	6,000		
9	49	..	....	5,800	76	Tuberculous laryngitis.
10	43	..	....	5,800	85	Before test breakfast, 8,600. After test breakfast, 12,400.
11	42	..	....	4,800	80	
12	64	..	5,264,000	4,600	70	

DILATED STOMACH

In many cases proteid absorption is so faulty that the blood is severely starved, but the *anæmia* may be concealed by the *concentration* of the blood brought about by the constant vomiting of large amounts of fluid. Kussmaul has shown that patients *often vomit more fluid than they ingest*, and it is obvious what must be the drain of this process on the fluids of the blood and all other tissues.

leucocytosis is often absent, as in cancer or chronic

CORROSIVE GASTRITIS.

blood was examined in a case of this kind in 1895 at the
etts General Hospital with the following result: Red
,000; white cells, 32,500; hæmoglobin, 53 per cent.

DISEASES OF THE INTESTINE.

FLUENCE OF SALINE CATHARTICS ON THE BLOOD.

[1] gives the following figures, showing the effect of sulphate
um in concentrating the blood: Healthy man of thirty-three,
Red corpuscles, 5,025,000; given 85 c.c. of a concen-
olution of sulphate of sodium in water; thirty-five minutes
d count showed red corpuscles, 6,540,000; sixty-five
ater blood count showed red corpuscles, 6,790,000; four
r blood count showed red corpuscles, 4,930,000. Evi-
ich fluid was drawn out of the blood-vessels, and then
our hours the tissues had supplied the loss and the blood
had returned to its normal density.

Hay also showed that dilute solutions of the same salt had far less effect in concentrating the blood. Further he demonstrated that if the blood is *already concentrated* when the saline is given, no purgative effect follows.

Grawitz confirms these results; he found also that common salt still further concentrates the blood (hence its production of thirst), and considers that (as this concentration accelerates *coagulation*) the household use of salt water as a remedy to stop hemorrhage is well founded.

ACUTE DYSENTERY.

(Shiga's bacillus) (see page 539).

ACUTE ENTERITIS.

Practically the great majority of cases of acute enteritis are part of a gastro-enteric attack, and in Table XLIV. (see page 322) the two have been lumped together. What was said of that table (page

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[1] Hay: "The Action of Saline Cathartics." Journal of Anatomy and Physiology, 1882, p. 430.

323) need not be here repeated. Besides the slight leucocytosis there mentioned, we may find in cases in which the stools are very watery a temporary concentration of the blood with increased specific gravity and red corpuscles. In infants the lymphocytes are apt to be increased at the expense of all the other varieties.[1] Eosinophiles may be absent. Thus in a case of subacute colitis following an attack of influenza pneumonia, Woehnert found ninety-seven per cent of lymphocytes in a total count of 14,000 white cells. The other three per cent were polynuclear.[2]

TABLE XLVI.—ENTERITIS, COLITIS, AND DYSENTERY.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	44	..	....	23,100	90	January 10th. Enteritis
				23,800	..	January 18th.
				29,100	..	January 19th.
				30,200	..	January 21st.
				16,700	..	January 23d.
				15,900	..	January 27th.
2	22	..	....	19,400	80	September 15th Chronic entero-colitis.
				17,800	..	September 17th
				25,400	..	September 19th.
				24,200	..	September 20th.
				21,000	..	September 24th.
				27,200	..	September 27th
				14,600	..	October 10th.
3	45	M.	3,840,000	17,000	50	August 26th. Chronic dysentery
				14,300	..	September 3d.
				7,700	..	September 5th. Dysentery ceased.
				8,800	..	September 20th.
4	25	F.	....	17,000	..	Chronic entero-colitis.
5	26	..	....	14,800	50	September 7th. Acute.
				7,600	..	September 9th.
6	Adult.	M.	3,624,000	13,000	58	Chronic entero-colitis.
7	33	..	....	12,600	90	Chronic.
8	Adult.	M.	4,320,000	12,400	..	Ulcerative colitis.
			2,732,000	10,600	..	Two weeks later.
			4,488,000	6,000	..	Three weeks later much improved.
9	39	F.	6,776,900	8,900	100	Acute febrile dysentery; bloody movements every hour.
10	3	F.	4,800,000	7,900	..	Ulcerative colitis.
11	40	..	....	7,800	30	
12	Adult.	M.	4,100,000	7,560	72	Chronic enteritis.
13	27	M.	4,872,000	7,000	..	Chronic diarrhœa and tetany.
14	20	M.	5,008,000	6,460	39	Chronic diarrhœa (tuberculous?)

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[1] But a summer diarrhœa without signs of colitis Zahorsky (N. Y. Med Journ., 1903, vol. 78. p. 505) finds the polynuclears increased and the lymphocytes diminished in proportion to the severity of the case.

[2] Journal of the American Medical Association. February 2d, 1901

XLVI.—Enteritis, Colitis, and Dysentery (*Continued*).

.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
..	2,198.000	5,800	45	February 14th. Chronic tropical. Severe secondary anæmia.
	2,224,000	......	37	February 18th.
	2,484,000	......	34	February 25th.
	2,230,000	......	40	March 4th. Diff. count, 200 cells; Polynuclear, 49 per cent; lymphocytes, 33; eosinophiles, 17; myelocyte, 1; normoblasts, 2; megaloblast, 1.
	1,976,000	......	42	
..	... .	5,600	90	
M.	4,900,000	5,300	80	Bloody stools ten days.
M.	.. ....	5,200	80	Catarrhal entero-colitis
F.	2,996,000	5.000	87	Chronic colitis.
F.	4,500,000	5,000	70	Diarrhœa.
F.	3,920,000	5,000	70	Chronic colitis.
..	....	8 600	80	

CHRONIC DIARRHŒA.

(See Table XLVI.)

In acute diarrhœa the other tissues respond to meet the loss of fluid sustained by the blood, and the blood is soon normal again. But when this process goes on long, the body becomes so wasted that the blood must share in the starvation and the albuminoids are drained out of it, leaving it watery and poor in corpuscles. A patient of Grawitz after years of chronic dysentery had but 1,880,000 red cells per cubic millimetre, while the serum had twice the normal amount of water and half the normal amount of solids. I have seen the count fall as low as 1,928,000 in a case of prolonged colitis, with final recovery. In another case the red cells reached no lower than 2,440,000, but the hæmoglobin was only ten per cent. A differential count of this man's blood showed the following:

	Per cent.
Polymorphonuclear neutrophiles	66.3
Lymphocytes (small)	24.9
Lymphocytes (large)	6.0
Eosinophiles	1.4
Myelocytes	1.4

While counting 400 leucocytes I saw 8 normoblasts and 5 megaloblasts. The total leucocyte count was 9,800 per cubic millimetre.

Cases 8, 15, and 19 of the series in Table XLVI showed similar conditions. The hæmoglobin, however, usually suffers most, and the color index is low.

Leucocytosis is rare, but does occasionally occur, possibly owing to some complication or auto-intoxication.

TABLE XLVII.—INTESTINAL OBSTRUCTION.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	1 mo.	..	....	34,200	..	Intussusception, died.
2	....	..	....	22,100	..	Twenty-first day, strangulated hernia.
				21,700	..	Twenty-second day, autopsy.
3	....	..	8,120,000	20,800	..	Cancer.
4	52	M.	5,568,000	18,860	..	May 6th, cancer.
				18,800	..	May 17th, cancer.
5	65	..	....	15,400	85	
6	Adult.	M.	....	14,666	..	No fæces three days.
						No urine two days.
				12,400	..	One day later, no fæces; urine drawn by catheter.
				4,100	..	Three days later, bowels moved six times.
7	47	..	....	13,300	75	
8	50	F.	....	12,200	..	Cancer of uterus.
9	35	M.	3,504,000	12,000	..	Chronic obstruction with hemorrhage.
10	21	M.	5,150,000	12,000	..	Obstruction (by a band).
11	56	F.	4,440,000	12,000	52	Cancer.
12	57	F.	4,272,000	11,000	75	Cancer.
13	Adult.	M.	5,800,000	6,800		
14	45	..	....	6,600	60	Double ovarian cyst.
15	72	M.	4,850,000	6,000		
16	29	..	....	6,000	..	Obstruction by band: operated.
17	58	..	4,480,000	5,800	90	Cancer.
18	Adult.	M.	5,200,000	4,000		
19	Adult.	M.	5,540,000	4,000		

Cholera is discussed on page 231.

For *Appendicitis* see Abscess, page 245.

INTESTINAL OBSTRUCTION.

Cushing[1] in 1898 first noted the leucocytosis (presumably toxæmic) associated with intestinal obstruction.

Bloodgood's[2] conclusions are as follows:

Within a few hours of the occurrence of obstruction the leucocytes rise rapidly. If obstruction is partial the counts are between

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[1] Cushing: J. Hopkins Bull., November, 1898.

[2] Bloodgood: Prog. Méd., December, 1901.

,000; if complete usually 20,000 or more. The higher unt and the shorter the duration the greater the probability of me. If there is a count of over 20,000 within the first twenty-urs, the chances are that gangrene is present. On the second counts do not change much. Then if gangrene or peritonitis he count begins to fall, otherwise the count remains high until th or fifth day, when the leucocytes gradually fall whatever dition of the abdomen. If after three days of obstruction the still over 20,000, the prognosis is good. If the count is be-000, the probability is that gangrene, peritonitis, or fatal oxication has occurred. Bloodgood thinks the leucocyte count t value on post-operative complication suggesting obstruction

DISEASES OF THE LIVER.

CATARRHAL JAUNDICE.

e serum is colored yellow or greenish-yellow and contains bile ents in solution. It has been asserted that jaundice can be gnized here before it shows in the skin or urine. In mild cases, when some bile goes to the intestine and the obstruction is not of long standing, *the blood is practically normal*, as the cases in Table XLVIII. show. Achard and Loeper[1] studied twenty-four cases of jaundice of various origins and found in the catarrhal type at the beginning a slight polynuclear leucocytosis; at the end a low percentage of polynuclears with slight eosinophilia.

TABLE XLVIII.—CATARRHAL JAUNDICE.

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
47	..	....	14,700	..	Seven weeks. Catarrhal (?).
25	..	....	11,100	85	
21	M.	....	10,500	81	
26	. •	....	10,400	60	
44	M.	....	10,200		
41	..	....	10,000	62	
25	F.	4,810,000	10,000	77	
			10,000	90	
			8,000		
30	F.	....	9,600	68	
34	..	....	9,200		
42	M.	2,896,000	8,775	47	Alcoholic gastritis.
40	..	....	8,200	75	
			8,100		

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[1] Achard and Loeper: Soc. de Biol., 1901, p. 217.

TABLE XLVIII.—CATARRHAL JAUNDICE (*Continued*).

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
40	..	....	8,000		
28	..	....	8,000		
87	..	....	7,500		
80	..	....	7,500		
26	M.	... .	7,500		
21	M.	4,800,000	7,500	65	
44	..	....	7,500	70	
80	M.	... .	7,400	64	
30	M.	... ...	7,800		
48	..	8,080,000	7,000	45	August 13th.
			7,240	..	August 14th.
53	M.	4,240,000	6,793	79	
24	..	....	6,800		
44	.	... ..	6,200	..	Obstruction.
29	M.	....	6,200	82	
..	M.	4,996,000	6,000	78	
24	..	....	6,000	78	
28	.	.. ....	5,500	90	
25	.	....	5,400	80	Polynuclears, 78 per cent; lymphocytes, 19; eosinophiles, 1; myelocytes, 0.75; 1.25 (?); reds pale, deformed; 1 normoblast.
24	..	....	5,400	90	
82	..	....	5,800	..	March 16th.
		5,600,000	4,700	75	
35	M.	4,850,000	4,900	85	
44	.	8,168,000	4,800	85	
29	F.	....	4,200	85	
			9,600		
19	F.	....	4,000		

Only one of these cases shows any leucocytosis, and the red cells and hæmoglobin have not suffered except in the alcoholic case in which other causes for anæmia were present. This is contrary to the observations of Grawitz, who constantly found leucocytosis, but agrees with those of v. Limbeck and Hayem, who never found any increase of leucocytes or any other changes in the blood count. Coagulation in this or any other type of obstructive jaundice may be very slow, but this is especially apt to be true in gall-stone cases even if no jaundice is present. Coagulation may be increased to eleven minutes (Osler) and patients may bleed to death during operation on gall stones. The amount of fibrin is normal. Von Limbeck noticed an *increased resistance* of the red cells to the influence of distilled water and dilute saline solutions which in normal blood dissolve the hæmoglobin. He asserted also that the *size* of the red corpuscles was *greater than normal*, their volume in a given blood being seventy-seven to eighty-one per cent (*i.e.*, p seventy-seven to eighty-one per cent of the room occu- by the drop), while the normal is about forty-four per cent.[1]

Qualitative Changes.

witz noted in severe cases that crenation took place much rapidly than usual in freshly drawn blood, and that the rou- formation did not take place. This latter point was also d by Hofmeier[2] in icterus of the new-born. Silbermann[3] no- n the same disease great deformities in the size and shape of cells In severe febrile icterus Weintraud noted in the red the white spots and streaks with active (molecular) movements ribed by Maragliano (see page 79) as endoglobular degenerative nges.

Summary.

Occasionally there is slight leucocytosis at the onset, otherwise al blood, with some degenerative changes in severe cases.

Diagnostic Value.

The constant presence of leucocytosis excludes an uncomplicated "catarrhal" jaundice, and points to the probability of malignant disease or inflammation (cholangitis, abscess) Syphilis and cirrhosis of the liver might show the same condition of the blood From a severe cholæmia the absence of any marked anæmia and leucocytosis distinguishes a purely catarrhal case. (For the changes in cholæmia see page 339.)

CIRRHOSIS OF THE LIVER.

1. ORDINARY (ATROPHIC) CIRRHOSIS WITHOUT JAUNDICE.

In the early stages (according to Hayem) neither the red cells nor the hæmoglobin fall considerably. Most other observers (perhaps thinking chiefly of the later stages) report marked anæmia. In Da Costa's 18 cases the red cells averaged 3,404,000 and the hæmoglobin 47 per cent. Wlajew[4] counted from 3,000,000 to

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[1] Capps (Journ. Med. Research, December, 1903) finds no such change.

[2] "Die Gelbsucht der Neugeborenen," Stuttgart, 1882.

[3] "Die Gelbsucht der Neugeborenen." Arch. f. Kinderheilk., 1887, p. 401.

[4] Ref. in Petersburger med. Woch., 1894, No. 43.

4,000,000 red cells. The count may be increased after a tapping in cases with ascites, owing to the concentration of the blood from the rapid refilling of the belly with serum. Grawitz, on the other hand, noticed precisely the opposite effect in a patient whose blood before tapping had been concentrated by cyanosis, the heart's action being embarrassed by the ascites. After tapping, when the heart's action had become easier and stronger, the cyanosis disappeared and the blood count fell from 4,700,000 to 4,300,000. In v Limbeck's case it rose from 4,680,000 to 5,160,000. The moral is that we should draw no inferences from the count of red cells soon after a tapping.

The forty-three cases in Table XLIX., A , were all advanced and their red cells averaged only 3,580,000 + per cubic millimetre. They steadily decrease as the disease progresses, one case getting as low as 1,300,000; but the anæmia may be concealed by cyanosis and concentration.

Qualitative Changes.

Hayem noticed spontaneous agglutination of the erythrocytes, a great tendency to adhere to each other. Von Limbeck looked for it, but could never find it. Hayem and Maragliano noticed degenerative endoglobular changes in the red cells ("*état cribriforme*").

Table XLIX., A.—Cirrhotic Liver without Jaundice.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	58	..	4,504,000	29,300	60	Temp. 100°. Delirium tremens.
				18,500	..	Fourth day.
2	35	..	908,000	26,000	20	Intestinal hemorrhage. Diff. count 500 cells: Polynuclear, 85 per cent; lymphocytes, 14; eosinophiles, 0.8; myelocytes, 0.2; normoblasts, 10; megaloblasts, 0.
			1,732,000	19,800	25	Seventh day. Diff. count 500 cells: Polynuclear, 88 per cent; lymphocytes, 10; eosinophiles, 1; myelocytes, 1; normoblasts, 2.
			2,456,000	16,900	23	Fourteenth day.
			3,098,000	14,000	35	Thirtieth day.
3	53	..	....	23,400	..	First day. Uræmic symptoms.
				5,800	..	Eleventh day. Autopsy.
4	34	..	....	18,900	58	December 21st.
				8,400	..	December 23d.
			4,000,000	.. ...	..	December 24th.
5	51	..	....	18,200	30	Hæmoptysis. Autopsy.
6	53	F.	2,950,000	16,000	..	Recent hemorrhage.

IX., A.—Cirrhotic Liver without Jaundice (*Continued*).

			Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
		..	....	14,000	..	Tapped; 328 ounces.
		..	3,000,000	13,000	55	With mitral disease.
		M.	4,300,000	12,700	55	Liver enlarged. Ascites.
		.	....	11,800		
		..	....	11,600	60	Autopsy.
		..	4,896,000	11,500	50	
		..	....	10,500	60	
		..	....	10,000		
		..	4,052,000	9,800	55	
		M.	4,992,000	9,000	62	Recent hemorrhage.
		M.	2,120,000	9,000	23	March 15th.
			1,300,000	7,500	22	April 8th.
					15	April 18th.
					15	April 29th.
			2,350,000	6,000	20	May 10th.
			2,375,000	5,300	26	May 12th.
			2,450,000	5,200	20	June 10th.
			4,500,000	7,800	25	June 16th.
		..	....	9,000	62	Hypertrophy.
		..	3,100,000	8,400	45	
		M.	3,440,000	8,320	46	Liver enlarged.
		M.	....	7,900	95	
	49	..	....	7,800	..	Tapped; 144 ounces.
	38	..	5,360,000	7,600	55	
	56	M.	....	7,500	68	
25	47	..	....	7,500	70	
26	64	..	....	6,400	85	
27	57	..	3,744,000	6,400	58	
28	43	..	2,620,000	6,200	35	
29	53	..	....	6,200	60	
30	48	..	4,888,000	6,100	65	
31	38	F.	....	5,700	65	
			5,720,000	5,200	46	Differential normal count.
32	45	..	2,830,000	5,500	40	
33	14	..	3,480,000	5,500	55	
34	54	M.	....	5,400	64	
35	46	..	....	5,200	80	
36	56	M.	4,680,000	5,000	48	Liver atrophic, July 12th.
			4,312,000	4,000	62	July 25th.
37	42	M.	2,920,000	4,500	56	October 30th.
				13,400	..	November 7th, during digestion.
				15,300	..	November 11th, during digestion.
38	53	M.	....	3,800	72	
39	54	F.	....	3,300	65	
40	63	M.	3,844,000	3,000		
41	45	..	....	2,600	80	
42	50	M.	3,568,000	2,400	50	
43	52	M.	3,440,000	2,400	50	

Hæmoglobin.

Usually the color index is low; the average was 0.66 in the ten Massachusetts General Hospital cases.

White Cells.

Except during severe nervous manifestations of toxæmia and after recent hemorrhage none of our cases showed any leucocytosis and the average count was 7,240, some cases having notably low figures (2,400, 3,000, 4,500).

Hayem's and Da Costa's results agree with mine Von Limbeck makes no definite statement. Rosenstein and Wlajew found leucocytosis, the latter 12,000 to 17,000. Possibly their cases include the forms of cirrhosis *with* jaundice in which (see Table XLIX., B) the white cells are more often increased.

The forms of hypertrophic cirrhosis *without* jaundice are here classed with the atrophic cases whose blood has just been described.

TABLE XLIX., B.—CIRRHOTIC LIVER WITH JAUNDICE.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	54	..	....	36,400	85	Death.
2	29	..	3,700,000	20,000	30	Toxic symptoms. Delirious.
3	42	M.	1,024.000	19,600	36	Autopsy.
4	38	M.	3,400,000	19,500	50	
5	32	..	2,392,000	19,300	55	Syphilis.
6	51	..	3,960,000	19,200	47	Hæmoptysis. Delirious. Death.
7	32	..	....	18,200	65	Temp. 102°-104°. Liver enlarged.
8	36	..	....	15,600		
9	45	M.	....	14,000	65	Liver enlarged.
10	49	..	4,228,000	13,000	55	July 14th.
				34,500	..	July 23d. Autopsy.
11	28	..	....	12,400	65	Ascites.
12	57	.	....	12,200	63	
13	35	..	5,016,000	12,000		Liver enlarged.
14	29	..	....	11,600	85	
15	57	..	....	10,500	85	Atrophic.
16	43	..	....	10,000	78	
17	54	..	....	9,300	..	Ascites.
18	58	..	2,640,000	8,800		
19	33	..	3,740,000	8,700	50	Differential count, 400 cells: Polynuclear, 87 per cent; lymphocytes, 12; eosinophiles, 1; normoblast, 1.
				19,200	..	Twentieth day. High fever, toxic symptoms.
				22,000	..	Twenty-fourth day. High fever, Toxic symptoms. Autopsy.
20	49	..	....	8,600	85	
21	52	..	....	8,600	70	
22	65	..	....	8,100	75	Hypertrophic.
23	65	..	....	7,800	80	
24	65	..	....	6,300	64	Hypertrophic.
25	34	..	3,868,000	5,250	58	

LIX., B.—Cirrhotic Liver with Jaundice (*Continued*)

Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
3,872,000	4,600	60	April 29th.
3,640,000	.... ..	62	May 6th.
3,944,000	....	63	June 13th.
2,064,000	4,300	50	Jaundice only transient.
2,904,000	2,400	54	Autopsy (hypertrophic cirrhosis).
....	......	..	Polynuclear cells, 83 per cent; lymphocytes, 17%.

2. Hanot's Cirrhosis.

Red Cells.

True (biliary) hypertrophic cirrhosis *with* jaundice has, according ayem, an intense anæmia in many cases In others it has no effect on the blood than ordinary atrophic cirrhosis. I have r met with a case.

Hæmoglobin.

In a single case of this variety of cirrhosis Hayem found in four successive blood examinations a color index of more than 1. His counts are as follows:

Date.	Red cells.	White cells.	Per cent hæmoglobin.	Color index.
January 9th	1,599,600	....	41	1.27
January 11th	1,884,000	21,803	50	1.39
January 12th	1,798,000	18,082	50	1.46
January 15th	1,971,000	15,500	53	1.40

Dried specimens showed an increased average diameter of the cells as in pernicious anæmia. The patient died January 15th, and the autopsy confirmed the diagnosis of hypertrophic cirrhosis.

Only one of our cases of hypertrophic cirrhosis with jaundice showed this condition—Case 27 in Table XLIX., B. The corpuscles numbered 2,064,000, or 40 per cent, and the hæmoglobin 50 per cent, a color index of 1.25. This case was jaundiced at the time of the examination.

I have seen no confirmation of Hayem's observations by any other writer.

White Cells.

In Hanot's cirrhosis leucocytosis is apparently commoner than in the other varieties. Hanot and Mennier found from 9,000 to 21,800 leucocytes per cubic millimetre in five cases, and an average of 6,600 in ordinary cirrhosis. Among the 29 jaundiced cases of cirrhosis in my series, 14 (about fifty per cent) showed leucocytosis, due, I conjecture, to the relatively late toxæmic stage in which most of these cases were at the time the blood was taken. The toxæmia of fibrous hepatitis, like that of fibrous nephritis, is probably capable of producing leucocytosis. Similarly high counts were found in some of the non-jaundiced cases while in the toxæmic state.

Diagnostic Value.

The blood of either form of cirrhosis has no diagnostic value, so far as I know, except to exclude abscess and hydatids. If no leucocytosis is present, abscess and hydatid cyst can usually be excluded

HYDATID CYST OF THE LIVER.

The earlier observations which I have met with are those of Hayem and Neusser. Hayem states that the blood shows leucocytosis and increased fibrin. Neusser considers that the *increase of eosinophiles* which he finds in hydatids serves to distinguish them from hydronephrosis, dilated gall bladder, etc. Neusser's discovery of eosinophilia in hydatid disease has been abundantly confirmed of late. Memmi[1] in 12 cases found 10 to 18 per cent of eosinophiles; Darguin and Tribondeau[2] add one similar case, and others are mentioned by Achard and Clerc[3] (up to 40 per cent of eosinophiles) by Laubry[4] (10 per cent), and by Abbé[5] (4 per cent). Tuffier and Milian[6] give brief notes of 5 cases with 4 to 8 per cent of eosonophiles out of 10,000 to 15,000 leucocytes. Lépine[7] in hydatid of the liver counted 28,000 leucocytes with 18 per cent eosinophiles (4,500 absolutely).

Seligman and Dudgeon[8] report the following observations in hydatid of the liver:

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[1] Memmi: Ref. in La Sem. Méd., November 13th, 1901.

[2] Darguin and Tribondeau: Presse Méd., November 6th, 1901.

[3] Achard and Clerc: Ref. in Arch. Gén. de Méd., 1902, p. 743.

[4] Laubry: *Ibidem.* [5] Abbé: *Ibidem.*

[6] Tuffier and Milian: Soc. de Chirurg., February 25th, 1902

[7] Lépine: Soc. de Biol., March 8th, 1902.

[8] Seligman and Dudgeon: Lancet, June 21st, 1902.

Date.	Red cells.	White cells.	Per cent hæmoglobin.	Per cent eosinophiles.	Per cent polynuclear.	Per cent lymphocytes.	Per cent mast cells.	Remarks.
1901— Dec. 27th....	6,290,000	17,000	70	57.0	22.0	20.0	1.0	Before operation.
1902— Jan. 13th ...	....	7,000	....	12.0	59.0	28.0	1.0	Three days after draining cyst
Feb. 20th ..	....	....	....	1.0	60.0	29.0	1.0	Free purulent discharge.
March 13th..	2,934,000	7,000	....	3.2	73.2	22.2	1.4	More cysts evacuated.
April 3d	....	....	....	1.0	64.5	34.5	0	

Lougridge[1] reports a similar case with the following figures: Red cells, 4,400,000; white cells, 7,300: hæmoglobin, 84. Differential count: Polynuclear, 63.4; lymphocytes, 23.6; large myelocytes, 8.2; eosinophiles, 5.8 per cent.

In a second case with suppuration in the cyst the leucocytes were 18,000 with 1.4 per cent of eosinophiles (252 absolute).

Sabrazes[2] in 7 cases found always an increase in the eosinophile cells, sometimes slight and sometimes considerable; in tissues in the neighborhood of the cysts there was always a great accumulation of the eosinophile cells. It therefore appears that the echinococci have a positive chemotaxis toward the eosinophile cells. Polycytosis, polychromatosis, nucleated reds, or red cells with basophilic granules were not observed. Unually there was a leuocytosis, although sometimes it was not present.

From these records of over thirty cases it appears that *eosinophilia is the rule in hydatid disease without suppuration.* Only two negative cases are so far on record (Bezancon and Weil[3] and Gourand.[4] In three cases I recorded the following:

ECHINOCOCCUS CYST.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	31	3,664,000	8,650	48	Iceland.
2	..	....	11,000	95	
3	..	....	34,000		

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[1] Longridge: Brit. Med. Jour., November 8th, 1901.

[2] Sabrazes: Münch. med. Woch., March 31st, 1903.

[3] Bezancon and Weil: Arch. Gén. de Méd., 1902, p. 743.

[4] Gourand: Soc. Anatom., January 10th, 1900.

ACUTE YELLOW ATROPHY OF THE LIVER

Grawitz records a case with 5,150,000 red cells and 16,000 white cells.

A single case with autopsy was studied at the Massachusetts General Hospital in 1894, the blood showing 5,520,000 red cells, 12,000 white cells, and 60 per cent of hæmoglobin.

Ewing reports three cases with leucocytosis, 15,000 to 21,000. "The absence of rouleaux and early crenation mentioned by Grawitz were not noted."

PHOSPHORUS POISONING.

Taussig,[1] v. Jaksch,[2] Badt,[3] and v. Limbeck[4] note an *increase* in the normal number of red cells per cubic millimetre. Taussig found 8,650,000 per cubic millimetre; Badt, 6,400;000, 6,500,000, and 6,800,000 in three successive cases; v. Limbeck, 6,500,000 and 7,900,000. That this increase is not due to concentration of the blood through vomiting of liquid is proved by v. Limbeck's last case, in which no vomiting whatever took place.

The count usually falls to normal within a few days. All these changes were verified in thirty-three cases at the Stockholm Hospital in 1892 (see Stockholm reports for 1892).

The white cells in v. Limbeck's second case were increased to 12,500. In v. Jaksch's five cases the counts were 58,750, 48,000, 8,000, 4,070, and 3,400.

TOXÆMIA IN HEPATIC DISEASE ("CHOLÆMIA").

When jaundice is intense and of long standing, as in complete obstruction of the bile ducts by gall stones or tumors, the blood is weakened very notably, and hæmoglobin and the count of corpuscles fall steadily. Very little is to be learned upon the subject from the literature, but the qualitative changes mentioned under catarrhal jaundice are much more marked, and leucocytosis is apt to be present. I have studied the blood in one case of fatal chronic jaundice without fever and for which at autopsy no cause was found. The leucocytes ranged between 12,000 and 14,000.

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[1] Arch. f. experiment. Path. und Pharm., vol. xxx.

[2] Deut. med. Woch., 1893, p. 10.

[3] Dissert., Berlin, 1891.

[4] *Loc. cit.*, p. 34.

GALL STONES.

Netter[1] and Sittmann[2] found pyogenic organisms in cultures from the blood of patients with gall stones, as have Gilbert and Girode[3] and others. The *slow coagulation* is of great surgical importance. Da Costa in 38 cases found that "gall stone does not of itself excite leucocytosis"; acute inflammatory complications raised the count in about one-third of his cases. The maximum in 28 cases was 18,800, the average 10,100.

Of the 50 cases of this disease examined at the Massachusetts General Hospital 2 were complicated with cholangitis (see Table L., A) Excluding these 2, marked leucocytosis was present in only 5 of 50 cases. The red cells were low in 2 cases (2,800,000 and 3,900,000).

The absence of leucocytosis helps us to distinguish the disease from peritonitis and appendicitis, and to exclude suppurative cholangitis.

TABLE L., A.—GALL STONES.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	25		....	28,200		
2	39	F.	4,768,000	24,000	..	Cholangitis also.
3	34	..	....	24,000	80	May 7th. Hydrops of gall bladder.
				26,400	..	May 8th.
				22,000	..	May 10th.
4	30	F.	4,820,000	20,000	..	Cholangitis. Autopsy.
5	63	F.	4,610,000	18,800		
6	29	M.	....	16,200	..	December 16th.
				13,200	..	December 18th.
				10,000	..	December 21st.
7	60	..	....	14,300	..	First day. Pus in gall bladder.
				20,700	..	Fourth day.
				15,000	..	Fifth day. Operation.
8	40	F.	4,520,000	13,000		
9	60	F.	....	12,500	72	Temp. 100.5°.
				11,500	70	
10	24	..	....	12,000	80	Hydrops of gall bladder.
11	25	..	....	11,600		
12	46	..	4,176,000	11,400	45	
13	63	..	....	11,300	..	Obstructive jaundice.
14	39	..	4,168,000	10,500	65	No pain.
15	37	..	....	10,300	..	In colic.
16	40	M.	....	10,250		
17	60	..	4,336,000	10,200	45	
18	55	..	....	10,200	..	In pain.

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[1] Progrès Médical, 1886, No. 46.

[2] Deut. Arch. f. klin. Med., 1894, p. 323.

[3] La Semaine Méd., 1890, No. 58.

TABLE L., A.—GALL STONES (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
			4,448,000	10,000	58	Sixth day. Operation.
19	60	..	....	10,200	90	Hydrops of gall bladder.
20	49	F.	....	10,000	90	Jaundice.
21	40	..	....	9,900		
22	47	..	....	9,800	85	
23	56	..	....	9,700		
24	41	..	....	9,400	90	No pain.
25	32	..	....	9,400	..	No pain for two days. Temp. 100°.
26	33	..	....	9,400	..	Colic.
				5,200	..	Colic.
27	32	..	....	9,200	..	No colic.
28	45	F.	....	9,200	100	
29	38	F.	....	8,900	60	Distended gall bladder.
30	25	F.	5,072,000	8,800	..	Jaundice.
31	40	..	....	8,300	..	No pain.
32	46	..	....	8,200	..	Colic.
33	27	..	....	8,200	..	Day after colic.
34	22	M.	3,288,000	8,000	..	Jaundice.
35	25	F.	4,900,000	8,000		
36	54	..	....	7,800	..	Between attacks.
37	50	..	....	7,700	..	Deep jaundice.
38	37	..	....	7,600	60	
39	54	F.	....	7,600	80	
40	40	..	....	7,400	60	August 25th.
				3,700	..	August 27th.
			4,336,000	11,500	50	August 31st.
				15,100	..	September 6th.
			3,636,000	10,600	40	September 7th.
41	48	..	....	7,400		
42	29	F.	2,844,000	7,400		
43	57	F.	....	7,400	85	
44	37	F.	....	7,300	..	October 1st.
				8,200	..	October 5th.
45	48	..	....	6,700	..	Between attacks.
46	58	M.	....	6,000	64	
47	57	F.	....	5,400	68	
48	51	F.	....	5,300	63	
49	28	..	....	5,200	..	In colic, proved at operation.
50	24	M.	4,320,000	4,000	..	Recurrent pain and jaundice.

WHITE CELLS AT ENTRANCE.

Between 2,000 and 6,000 = 5 cases.
" 6,000 " 8,000 = 15 "
" 8,000 " 10,000 = 21 "
" 10,000 " 12,000 = 12 "
" 12,000 " 14,000 = 4 "
" 14,000 " 16,000 = 7 "

Between 16,000 and 18,000 = 4 cases.
" 18,000 " 20,000 = 2 "
" 20,000 " 30,000 = 3 "

Total............ 73 "
Average number of white cells, 10,000 +

CHOLANGITIS AND CHOLECYSTITIS.

e the leucocytosis is well marked whenever the inflammation
beyond the catarrhal stage (see Table L., B), and helps
clude simple impacted gall stone, with or without colic.
y or may not produce leucocytosis, but does not usually
he fibrin network. It is said by Hayem that cholangitis
ot increase it.
good (*loc. cit.*) concludes that "in acute cholecystitis the
es invariably rise to from 20,000 to 27,000." If no opera-
one and the local symptoms abate, the count falls. In chronic
titis (8 cases) the leucocytes were from 5,000 to 12,000
mal). "In cholecystitis with jaundice and stone in the
on duct" (8 cases) the leucocytes were normal (2,000 to 10,-
One patient observed from the beginning of an acute at-
showed a rising leucocytosis, which reached 24,000 and then
fell to 9,000 as the acute local symptoms subsided. Jaundice persisted and at operation a stone was found in the common duct.

TABLE L., B.—CHOLANGITIS.

No.	Age.	Sex.	Red cells.	White cells.	Remarks.
1	....	F.	4,800,000	50,000	Suppurative cholangitis.
2	....	F.	6,400,000	30,000	
3	....	F.	4,960,000	22,000	
4	21	M.	4,976,000	14,800	Jaundice and cholæmia.
5	65	M.	....	14,186	Gall-stones ; chills.
6	....	....	....	11,000	October 20th. Operation October 22d. Abscess of liver.
7	28	M.	6,640,000	9,000	Catarrhal.
			5,592,000	6,800	
8	34	F.	4,770,000	4,400	Catarrhal.

TABLE L., C.—CHOLECYSTITIS.

No.	Age.	Red cells.	White cells.	Per cent. hæmoglobin.	Remarks.
1	24	.. ....	26,600	80	November 3d. Suppurative
			26,400	..	November 4th.
2	48	....	23,000	..	First day. Infectious.
			15,500	..	Third day.
3	36	....	22,600	60	Suppurative

TABLE L., C —CHOLECYSTITIS (*Continued*).

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
4	32	....	15.600	73	Gall stones.
5	47	....	14.100	75	July 14th.
			17,000	..	July 17th.
6	25	....	12,200	60	
7	58	....	10,700	80	
8	28	....	8,500	90	
9	50	....	8.300		
			46,300	..	Ten days later. Suppurative.
10	44	3.602,000	6,600	50	Typhoid.
11	47	....	6,400	75	Chronic. Diff. count 400 cells: Polynuclear, 69 per cent; small lymphocytes, 29; large lymphocytes, 1.5; eosinophiles, 5.

The blood does not differ from that of cholangitis with suppuration.

ABSCESS OF THE LIVER.

In most acute cases leucocytosis is well marked (as in 5 of my 8 cases), but in the chronic latent cases when we most need the assistance which leucocytosis might give in diagnosis, it is often absent altogether. Thus Osler[1] in 5 cases found: Case I. 6,000 to 11,000; Case II. 8,000 to 11,000; Case III., 9,000; Case IV., 15,000; Case V., 22,000. Scott[2] reports on 3 cases and finds that the leucocytosis is valueless for diagnosis since it is present only in early acute stages when other clinical data suffice, and in chronic cases is slight or absent. Cohen[3] reports 13,400 in a chronic case with several quarts of pus. Delaney (see reference page 472) in 3 cases found 15,400, 15,700, and 12,500. Boinet's[4] 2 cases were acute and showed well-marked polynuclear leucocytosis.

Futcher[5] reports that the average blood count in fifteen cases of amœbic dysentery complicated by abscess was as follows: red cells, 4,250,000; leucocytes, 18,350, and hæmoglobin 66 per cent. "The leucocytosis was not a high one. The average was 7,750 higher than in the uncomplicated dysentery cases. There were two cases

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[1] Osler: Med. News, April 12th, 1902

[2] Scott: Trans. College of Phys., 1902, p. 174.

[3] Cohen: *Ibidem*, p. 170

[4] Boinet: Soc. des Hôp., 1900, p. 1089.

[5] Futcher: Journ. Am. Med. Assn., August 22d, 1903.

highest count was under 10,000. The highest leuco-
sis of all was 53,000.

"Some observers hold that there is a great increase in the leuco-
es in cases of aœmbic hepatic abscess and emphasize its impor-
ce in the diagnosis of such cases. Few, however, give counts
porting their statements. Although this series shows that the
rage leucocyte count in the amœbic abscess cases is considerably
ve that in the uncomplicated cases, yet it is doubtful whether
leucocyte count is of any great value as a means of diagnosis.
instance, in the forty-three uncomplicated dysentery cases there
e ten in which the leucocyte count was above the average in the
ess cases. In two of these the counts were 40,000 and 47,000
spectively.

"The average differential count of the leucocytes showed a rela-
tive increase in the polymorphonuclears. Considering the rather
rge number of eosinophiles seen in the stools in certain cases, it
s thought that there might be some change in the relative per-
ntage of these cells in the blood. With the object of determining
ether there was such a change or not, Dr. McCrae made differen-
ual counts in a number of cases, but found the eosinophilic cells
present in practically normal percentages."

TABLE LI.—ABSCESS OF THE LIVER.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	20	M.	4,533,000	33,200	..	January 11th.
				48,000	..	January 14th. Operation.
2	15	F.	3,750,000	26,800	..	Operation.
3	55	..	....	18,900	85	Multiple. December 17th.
				23,400	..	Perihepatitis. December 19th.
				25,900	..	December 20th.
				27,000	..	December 21st.
				17,300	..	December 23d.
				28,400	..	December 25th.
				24,400	..	December 26th.
				15,000	..	December 27th.
				16,800	..	December 29th.
				18,000	..	January 3d.
				16,800	..	January 5th.
				16,200	..	January 7th.
				16,400	..	January 9th.
				18,000	..	January 11th.
				16,600	..	January 13th.
				11,700	..	January 15th.
				21,900	..	January 25th.
				30,600	..	January 27th.

TABLE LI.—ABSCESS OF THE LIVER (*Continued*)

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
				26,000	..	January 29th.
				32,000	..	January 31st.
				28,000	65	February 3d.
				31,000	..	February 5th.
						February 7th. Operation.
						February 13th. Death.
4	60	F.	4,460,000	18,000		Operation
5	28	M.	....	12,600		
6	33	F.	....	11.000	..	November 3d.
				17.500	..	November 4th, 11 A.M.
				19.200	..	November 4th, 2 P.M.
				20,600	..	November 5th, 10 A.M. Operation; autopsy.
7	26	M.	2,664,000	10.200	33	October 19th.
				12.000	..	October 20th.
				15,000	..	October 21st. October 25th, autopsy; streptococci.
8	51	F.	3,440,000	9,600		

CANCER OF THE LIVER.

(See Malignant Disease, page 440.)

GUMMA OF THE LIVER.

Von Jaksch in a single case found 2,756,000 red cells, 6,100 white cells; in similar cases I found 8,900 leucocytes and Grawitz 17,000.

DISEASES OF THE PANCREAS.

HEMORRHAGIC PANCREATITIS.

Opie records a leucocytosis of 19,600 in a case operated on by Bloodgood (*Johns Hopkins Bulletin*, January, 1901).

At the Massachusetts General Hospital we have had four cases in which the following counts are recorded:

ACUTE HEMORRHAGIC PANCREATITIS

No.	Age.	White cells.	Per cent hæmoglobin.	Remarks.
1	..	9,200		
2	26	11,200		
3	50	23,000	100	
		24,000	...	Fourth day.
4	..	22,000		

CHRONIC PANCREATITIS

d cells.	White cells.	Per cent hæmoglobin.	Remarks.
38,000	5,600	52	November 5th. Diff. count: Polynuclears, 56 per cent; small lymphocytes, 36; large lymphocytes, 6.5; eosinophiles, 1.5.
00	3,500	50	November 15th.
			November 18th.
	4,500	..	Before test breakfast.
	6,100	.	Four hours after test breakfast.
32,000	2,600	45	November 26th. Diff. count 500 cells: Polynuclears, 56.4 per cent; small lymphocytes, 35.2; large lymphocytes, 6.8; eosinophiles, 1.6.
	....	47	December 16th.
	....	50	December 29th.
	5,000	48	January 3d.
		46	January 10th.

DISEASES AFFECTING THE HEART.

PERICARDITIS.

(See Inflammation of Serous Membranes, page 282.)

ENDOCARDITIS

In many cases of acute endocarditis the blood shows no changes. In others, whatever alterations there may be are covered up by those involved in the *rheumatic* arthritis associated with the endocarditis.

ULCERATIVE ENDOCARDITIS.

In *ulcerative or malignant endocarditis*, we may find the signs of a pyogenic infection (see page 237). Sometimes pyogenic cocci can be cultivated from the blood, and if present *may be of the greatest value in a diagnosis* always difficult to make.

Grawitz goes so far as to say that in doubtful cases repeated negative results of cultures from the blood make it unlikely that ulcerative endocarditis is present.

Sittmann[1] considers that important help may be given as to the position of the primary focus of infection by the nature of the organism present in blood cultures—*i.e.*, the pneumococcus pointing to the lung, the colon bacillus to the intestine, etc.

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[1] *Loc. cit.*

Red Cells.

As in all forms of septicæmia marked anæmia rapidly develops, more rapidly probably than in any other disease. The hæmoglobin loses about equally with the corpuscles, according to most observers since blood destruction is so rapid.

Further evidence of rapid blood destruction is seen in the hæmoglobinæmia often present.

Roscher (*loc. cit.*) records counts of 4,400,000 and 2,750,000, both fatal cases.

White Corpuscles.

Rieder reports a single case showing these variations:

	Temperature.	White cells.
January 2d, 1891	105°	17,000
" 3d, 1891	99°	18,700
" 8th, 1891	103°	15,500
" 10th, 1891	101.5°	18,000
" 12th, 1891	101.5°	21,300
" 18th, 1891	101°	18,800
" 22d, 1891	104.5°	18,000

February 11th, the patient died.

Pée found leucocytosis. Roscher in two cases found: Case I.: 8,800 leucocytes; the patient died in two days. Case II.: 16,800 and 12,000. Krebs in one case found: October 27th, 15,500; October 28th, 44,200; the patient died the same day.

Twenty-six cases were studied at the Massachusetts General Hospital with the following results:

TABLE LII.—ULCERATIVE ENDOCARDITIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.	
	21	..	....	34,300			
				39,200	....	Third day.	
				27,000	....	Tenth day.	
				47,600	....	Seventeenth day. Died twenty-first. No autopsy.	
				30,100	....	May 27th.	
				15,800	....	May 30th.	
				18,100	...	June 17th.	
2	8 yrs.	..	4,216,000	26,100	50	November 20th	Aortic stenosis. Mitral insufficiency.
3	11 mos.	..	....	27,000	....	November 23d	
				27,500	....	November 27th	
				27,400	....	December 3d	
				25,000	....	December 9th	
				16,600	....	December 22d	

T BLE LII.—Ulcerative Endocarditis (*Continued*).

		Sex.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
				25,700	....	May 22d.
				27,840	....	May 24th.
				18,100	....	May 26th.
				22,000	....	May 28th.
		..	....	24,500	80	December 15th. Acute malignant; pneumococci; chronic fibrous endocarditis; mitral regurgitation; resolving pneumonia; autopsy.
				21,300	....	December 18th.
				16,300	....	December 20th.
				22,000	....	December 22d.
		..	....	22,800		
		..	....	22,700		
				20,400	....	Autopsy.
		..	....	20,300	75	(Six months' fever.)
		..	....	20,100	80	July 31st.
				13,500	....	August 4th.
				10,900	....	August 6th.
				17,400	....	August 16th.
			4,976,000	15,900	70	August 17th. Diff. count 200 cells. Polynuclear, 89.5 per cent; small lymphocytes, 6; large lymphocytes, 4; eosinophiles, 5.
				12,900	....	August 22d.
				19,500	....	August 26th.
				32,300	....	August 27th.
				18,300	....	August 30th.
				17,100	...	September 1st.
				14,800	...	September 6th.
				13,600	....	September 9th. Autopsy.
9	29	..	....	19,100	....	Autopsy.
10	35	..	....	18,900	....	Pneumonia, January 28th, 1899.
				31,300	....	February 4th, 1900. No signs but a systolic murmur and chills.
				20,400	....	February 11th.
				20,900	....	February 15th.
				40,400	....	February 21st.
				31,000	....	February 23d.
				37,400	....	February 25th.
				63,700	....	March 1st.
				37,150	....	March 4th.
						March 7th. Autopsy. Malignant endocarditis.
11	63	..	....	18,800	....	April 7th T. 102°. Pneumonia.
				8,600	....	April 10th. Pneumonia gone. T. 99°.
			-	18,300	....	April 14th, 8 A.M. T. 104.5°. Aortic and mitral.
				29,200	....	6 P.M.
				35,800	...	April 15th, 7 A.M. Culture of blood (14th). Pneumococci.

TABLE LII.—ULCERATIVE ENDOCARDITIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
12	27		....	18,500	75	May 10th. Subacute glomerulonephritis. Autopsy.
				15,000	....	May 15th.
				12,000	....	May 17th.
				15,000	....	May 20th.
				11,000	...	May 23d.
				16,000	....	May 25th.
				18,000	....	May 27th.
				18,000	....	June 4th.
				19,500	....	June 6th.
				16,000	....	June 9th.
				11,000	75	June 13th.
				14,800	70	June 21st.
				13,000	....	June 29th.
13	34	..	....	18,000	80	February 13th.
				11,600	....	February 16th. Autopsy.
				21,400	....	February 19th.
				16,200	....	February 20th.
				1,600	....	February 23d.
				1,300	....	February 27th.
				24,400	....	March 3d.
14	23	.	....	17,800	....	April 22d. Death.
				36,800	....	April 25th.
				25,400	....	April 30th.
				25,000	....	May 2d.
				28,100	....	May 5th.
				29,400	....	May 7th.
15	35	.	2,718,000	15,200	25	Polynuclear, 86 per cent.
						Lymphocytes, 14 "
						Eosinophiles, 0 "
16	3 yrs. 11 mos.	..	....	18,500	....	No autopsy.
17	44	..	3,996,000	13.400	55	October 18th.
				18,000	....	October 22d.
				12,600	....	January 13th.
				14,500	....	January 14th.
				20,400	....	January 16th.
				24,000	....	January 18th; died.
18	21	..	5,330,000	11,300	45	January 8th.
				9,000		
				11,700	42	Pulmonary embolism.
				18.700	50	March 15th.
				13,900	48	April 6th. No autopsy.
19	30	..	....	11,000	70	April 2d.
				31,000	....	April 24th.
				16.000	....	April 26th.
20	....	..	3.792,000	10,000	58	
21	....	..	....	8,900	55	Autopsy.
22	30	..	....	8.460	82	February 23d. T. 101.4°.
				8,130	....	February 26th. T. 104.8°.
				6,880	....	February 27th. T. 103.5°. Death
23	28	..	....	7,900	....	Hyperplastic.
24	32	..	....	7,600	...	Autopsy.

ABLE LII.—ULCERATIVE ENDOCARDITIS (*Continued*).

e.	Sex.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
	..	3,884,000	5,200	45	December 15th. Polynuclear, 91.2 per cent. Lymphocytes, 6.7 " Eosinophiles, 2.1 "
			11,900	....	December 27th.
		4,272,000	....	50	December 31st.
			10,100	....	January 7th.
			8,800	....	January 14th.
		3,560,000	... .	....	January 15th.
			21,300	45	January 26th.
			15,100	....	January 30th.
			6,200	....	February 24th.
		2,852,000	9,800	35	March 8th. No autopsy.
3	..	3,652,000	3,000	50	Polynuclear, 77.0 per cent. Lymphocytes, 22.5 " Eosinophiles, .5 " No nucleated reds. Autopsy.

y the same are the counts in the following cases of benign" endocarditis with fever and rapidly shifting urs, the tenth complicating chorea in a boy of thirteen.

TABLE LIII.—"BENIGN" ENDOCARDITIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
1	56	F.	....	50,100	..	November 24th.
				35,800	..	November 27th.
				36,600	..	November 30th.
				22,800	..	December 7th.
2	23	..	1,424,000	31,600	25	December 10th.
			1,240,000	28,000	..	December 13th.
					20	December 15th. Death.
3	4	..	....	29,600	..	Twenty-first. Temp. 102°.
				28,500	..	Twenty-second. Temp. 98°.
				19,600	..	Twenty-fifth.
4	25	..	....	26,600	70	October 19th } Aortic and mitral disease; subacute glomerulo-nephritis. Autopsy.
				41,200	..	October 20th
				32,300	..	October 23d
				29,300	..	October 24th
				28,400	..	October 26th
				32,200	..	October 27th.
				27,300	..	October 28th.
				29,000	..	October 30th.
				24,200	..	November 3d.
				29,600	..	November 5th.
				28,200	..	November 8th.
				36,500	..	November 13th.

TABLE LIII.—"BENIGN" ENDOCARDITIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
5	28	..	....	24,800	..	Twenty-fourth.
				11,700	..	Twenty-fifth.
6	11	..	4,728,000	24,500	55	First day.
				17,700	..	Seventh day.
				14,000	55	Fourteenth day.
				15,100		
				10,800	55	
				10,100	34	
7	27	..	....	24,000	80	First day.
				16,000	..	Fourth day.
				13,600	..	Fifth day.
8	13	..	....	22,500	80	January 28th.
				15,200	..	February 1st.
				21,400	..	February 4th.
				18,400	..	February 8th.
				29,400	85	February 21st.
9	29	..	....	21,320	..	Pregnancy four months.
10	13	M.	....	20,600	62	May 26th. Temp. 102°-104°.
				17,900	..	May 29th.
				18,700	..	May 31st.
				16,800	..	June 3d.
				21,200	..	June 4th.
				27,400	..	June 8th.
				22,700	..	June 11th.
				24,200	..	June 13th.
				21,900	..	June 15th.
				26,100	..	June 17th.
				26,800	..	June 19th.
				17,400	..	June 23d.
				28,700	..	June 26th.
				21,200	..	July 2d (outdoors).
				21,300	..	July 4th. Left the hospital July 19th.
11	54	..	3,768,000	20,200	90	January 24th.
				24,400	..	January 26th. Autopsy.
12	17	..	....	19,800	..	December 16th. Mitral insufficiency. Renal colic.
				19,200	..	December 20th.
13	34	..	....	19,700	50	November 5th.
				12,900	..	November 7th.
				11,000	..	November 9th.
				10,500	..	November 12th.
				7,200	..	November 14th.
				14,500	..	November 22d.
				19,300	52	November 25th.
				14,200	..	November 28th.
				18,300	..	November 30th.
				14,400	..	December 2d.
				10,200	..	December 5th.
				24,000	..	December 8th.
				35,300	..	December 11th.
14	26	..	....	12,000	..	Salpingitis.

Diagnostic Value.

l cultures should never be omitted in cases of suspected
nt endocarditis. When positive they are of great value.
xcluding typhoid, malaria, and miliary tubercle the pres-
leucocytosis is important. I saw within a few months a
which several consultants had made the diagnosis of typhoid,
hich the presence of marked and persistent leucocytosis and
ence of a typhoid serum reaction convinced me that the case
of ulcerative endocarditis. This has since been verified.

MYOCARDITIS.

never stasis and disturbance of the circulation result from
s of the heart wall, blood changes identical with those de-
under Valvular Heart Disease are present. Otherwise the
iormal. The ordinary findings are shown in the following

TABLE LIV., A.—MYOCARDITIS.

	x.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	..	....	30,000	75	No autopsy.
	..	....	13,200	68	Mitral disease with broken compensation.
62	..	....	12,900		
53	..	4,944,000	11,800	45	Broken compensation. Chronic bronchitis.
60	..	....	10,700		
62	..	....	10,700	..	Mitral insufficiency.
75	..	....	8,800	..	Syncope. Chronic interstitial nephritis.
58	..	....	8,300	63	Progressive muscular atrophy. Arthritis deformans.
55	..	....	7,400		
68	..	....	7,200	..	Chronic interstitial.
67	..	....	6,700	..	Chronic interstitial.

TABLE LIV., B.

White cells.	Cases.
Between 4,000 and 6,000	2
" 6,000 " 8,000	11
" 8,000 " 10,000	11
" 10,000 " 12,000	12
" 12,000 " 14,000	7
" 14,000 " 16,000	7
" 16,000 " 20,000	3
" 20,000 " 26,000	5
Total	58
Average count of white cells	9,100

VALVULAR HEART DISEASE.

Grawitz divides valvular heart disease into three stages with corresponding blood conditions:

1. Stage of full compensation: blood normal.

2. Stage of *acute* failure of compensation: blood diluted (Oertel's "plethora serosa").

3. Stage of chronic stasis and cyanosis: blood concentrated for the most part; at times diluted as well.

1. A valvular lesion *per se* has no effect on the blood.

2. When compensation fails and blood pressure is lowered, we find (*especially in the venous blood*) that the fluid from the surrounding lymph spaces has made its way into the vessels and diluted the blood. The specific gravity falls, red cells and hæmoglobin are lower than before, while the white cells are unaltered, and the plasma is shown to be more watery than before, as well as of increased quantity per cubic millimetre. All these changes are less marked in capillary blood, and hence are *rarely observed*.

3. If the heart adjust itself partially to the increased work it has to do, and to the chronic passive congestion of the internal organs and at the periphery, the blood is concentrated, probably in part by transudations into serous cavities and lymph spaces, and in part by the increased excretion of moisture by the lungs. The specific gravity and the number of red cells are increased, *especially in the capillaries*, and to a less extent in the venous blood (the conditions being just the reverse of those in acute heart failure, stage No. 2). This is the condition usually found in heart disease with chronic venous stasis (passive congestion).

But this concentrated condition of the blood may be offset from time to time by fresh weakening of the heart and lessening of blood pressure, and the combination of the two conditions may result in a normal blood count.

The condition of concentrated peripheral blood with the count of red cells above normal is that most commonly seen in chronic heart disease with stasis.[1]

Von Limbeck finds that aortic lesions are more apt to show a normal or diminished blood count, while mitral disease is more apt to be accompanied by the temporary dilutions and long-standing concentration above described. He does not explain the cause of this, and it does not coincide with my cases. One of his patients with double mitral lesion showed a decrease of 1,170,000 red cells (from 7,500,000 to 6,330,000) after exertion. When the patient was quiet, the lesion was compensated; on exertion compensation temporarily failed, blood pressure was lowered and the blood diluted.

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[1] Gibson (Brit. Med. Jour., January 17th, 1903) has recorded some striking cases illustrating this point.

Sadler[1] found considerable anæmia in three out of four cases of aortic disease, while only two of seven patients with mitral lesions showed anæmia.

Schneider's[2] results were similar in that he found the red cells normal in the aortic cases and increased in the mitral ones.

Hayem found anæmia most common in aortic regurgitation, especially in young people.

In the Massachusetts General Hospital records there have been a strikingly large number of cases of mitral disease associated with *severe* anæmia (see cases 2, 10, 14, and 88 of Table LV.). The counts of red cells in twenty cases average 3,400,000, and nucleated red cells were found in three cases. These were all of them *supposed* to be chronic cases without any active endocarditis, septic or benign, and were for the most part afebrile. In view of the marked anæmia and leucocytosis, however, I am in doubt whether the endocarditis was really as dormant as the temperature and the absence of chills or embolism would suggest.

In cases of aortic disease due to arteriosclerosis, there was no considerable anæmia or leucocytosis.

White Corpuscles.

Almost all writers whom I have consulted agree that the leucocytes are normal unless some complication occurs. Yet in a large number of the Massachusetts General Hospital cases the leucocytes were steadily *increased*, while the red cells were diminished (see Table LV.) This leucocytosis cannot be explained as the result of stasis, since it is rare in aortic disease or in myocarditis, despite stasis, and is found chiefly in mitral cases. That stasis plays a part in the blood counts of congenital heart disease seems evident from the cases next to be mentioned, in which the red cells are increased only about forty per cent, while the white are often one hundred per cent more numerous than normal.

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[1] *Loc. cit.*, p. 33.

[2] Inaug.-Dissert., Berlin, 1888.

The apparently normal count of red cells in some of our cases may have been due to the covering up of an anæmic or diluted condition of the blood by concentration, the resultant of the two forces being an apparently normal count.

In the 91 cases of mitral disease tabulated on pages 356–358, there are 51, or 56 per cent, showing leucocytosis of more than 11,000, and 32 with over 16,000 leucocytosis. In some of the cases there was pulmonary infarction or nephritis as a complication, and these lesions may have influenced the count.

The polynuclear cells are proportionately increased. In explanation of the anæmia and leucocytosis of mitral disease and the lack of these phenomena in aortic disease, I conjecture that mitral disease is rarely long dormant, and that the "failures of compensation," for which my cases sought the hospital, were associated with or due to fresh vegetative or thrombotic processes on the valves.

Œdema and diuresis have in themselves little or no constant effect upon the blood, as a recent observation of Petrowsky's has demonstrated.

CONGENITAL HEART DISEASE.

Vierordt[1] has collected the following table of cases of congenital heart disease showing extreme polycythæmia:

	Specific gravity.	Red cells.	White cells.	Per cent hæmoglobin.	Age.	Sex.
Toeniessen,[2] 1889	....	8,820,000	....	..	13	M.
Toeniessen,[2] 1889	....	7,540,000	....	..	10	F.
Krehl,[3] 1889	1.071	8,100,000	....	..	23	M.
Moritz,[4] 1892	1.081	7,900,000	8,800	150–170	24	F.
Vaquey,[5] 1892	....	8,900,000	....	..	40	M.
Bauholzer,[6] 1894	1.071	9,447,000	....	160	10	M.
Carmichael,[7] 1894	....	8,100,000	16,000	..	?	?
Hayem,[8] 1895	....	7,500,000	9,900	..	25	M.
Gibson,[9] 1895	....	8,470,000	12,000	110	8	M.
J. Thompson[10] (and Gibson)	....	6,700,000	12,000	92	2	M.

[1] Vierordt: Nothnagel's Specielle Pathologie und Therapie.

[2] Toeniessen: Dissertation, Erlangen, 1881.

[3] Krehl: Deutsch. Arch. f. klin. Med., 1889, p. 426.

[4] Moritz: Cited from Vierordt.

[5] Vaquey: Soc. de Biol., May, 1892.

[6] Bauholzer: Cent. f. inner. Med., 1894, p. 521.

[7] Carmichael: Edin. Hosp. Rep., 1894, vol. ii.

[8] Hayem: Méd. moderne, 1895, p. 397.

[9] Gibson: Lancet, 1895, vol. i., p. 24.

[10] Thompson: Cited by Gibson.

	Specific gravity.	Red cells.	White cells.	Per cent hæmoglobin.	Age.	Sex.
....	...	8,570,000	...			
....	1.077	6,800,000	....	..	18	F.
....	....	9,600,000	....	.	18	

isend[1] studied 14 cases. In 7 cases under one year the ere 11,800,000, 8,051,000, 8,000,000, 7,144,000, 6,580,000, , and 5,900,000. In 5 cases between the first and twenty-vear the counts were 9,950,000, 8,590,000, 7,590,000, and 6,000,000. In 2 cases the count was not increased; e showed no cyanosis.

such cases are to be explained I do not know; the ordinary of concentration of the blood will not hold in cases in stasis or lack of compensation exists, yet the skin is blue od counts are enormous.

s no doubt that the peripheral capillaries always contain orpuscles per cubic millimetre than do the veins. Numerous s from various observers agree upon this. Whether this is on account of the loss of water by perspiration and consequent drain of blood from the skin capillaries is uncertain, but in congenital heart disease both capillary and venous blood are overcrowded with corpuscles and the explanation is difficult. Hayem in a case of this sort reports 7,000,000 red cells with a *decrease* in the average diameter.

TABLE LV.—MITRAL VALVE DISEASE AND ITS COMPLICATIONS.

No.	Age.	Sex.	Red cells	White cells.	Per cent hæmoglobin.	Lesions.			Remarks.
						Mitral.	Aortic.	Tri-cuspid.	
1	26	...	....	44,000	70	M.	..	..	Died same day.
2	39	...	3,448,000	43,150	55	M.	A.	..	July 5th. Polynuclear, 71.4; lymphocytes, 27; myelocytes, 6; masts, 4.
			2,596,000	8,800	43				July 9th. July 10th, autopsy. Fresh and old endocarditis.
3	30	...	....	32,000	62	M. Ruptured comp.			
4	44	...	....	20,400	40	M.	..	..	Temp., 100°.
			4,480,000	27,000	..	....	..	..	Fifth day. Purpuric spots.

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[1] Nouillé: Thèse de Paris, 1896.

[2] Ruge: Berlin. klin. Woch., 1897, p. 429.

[3] Kovács: Cit. by Koranyi, Zeit. für klin. Med., 1887, vol. xxxi.

[4] Townsend: Archives of Pæd., September, 1899.

TABLE LV.—MITRAL VALVE DISEASE AND ITS COMPLICATIONS (*Continued*).

No.	Age.	Sex.	Red cells	White cells.	Per cent haemoglobin.	Lesions.			Remarks.
						Mitral.	Aortic.	Tri-cuspid.	
5	32	...	....	30,000	..	M.			
				19,000	..	....	..	..	First day with infarcts. Temp., 102°.
6	31	...	....	23,000	78	M.	..	T.	Third day. Died on fifth.
7	36	...	....	22,600	..	M. Double.	A.	..	No fever.
				22,600	..	....	..	..	Fourth day.
				24,600	..	....	..	..	Sixth day.
				19,000	..	....	..	..	Seventeenth day.
8	23	...	....	22,400	..	M.	..	T.	Pulmonary infarction.
9	8	...	....	22,100	..	M.			
10	8	...	2,624,000	22,000	35	M.	..	..	With nephritis. Polynuclear, 88; lymphocytes, 12; eosinophiles, 0; 2 normoblasts. (Count 500.) Died.
11	19	...	....	20,800	65	M. Stenosis.			
				11,700	..	....	..	..	Four days later. Temp., 96°.
12	25	...	3,756,000	20,700	35	M.	A. Double.	..	April 10th.
			3,680,000	13,000	35	....	..	..	April 20th. Temp., 104.6°. (Count 500.) Polynuclear, 86.6 per cent.; small lymphocytes, 8.6; large lymphocytes, 4.4; eosinophiles, .2; myelocytes, .2; 1 normoblast. No autopsy.
13	50	...	....	20,500	75	M.	..	..	Dilated and hypertrophied with pulmonary infarct.
14	16	F.	2,672,000	20,500	42	M.	A.	..	Acute nephritis.
15	76	...	....	20,400	..	M.	..	..	Cerebral embolism.
16	40	...	....	20,000	70	M. Double.			
				15,000	..	....	..	..	Third day.
				10,400	..	....	..	..	Seventh day.
17	45	...	3,244,000	19,900	35	M.	..	..	No autopsy.
18	39	...	....	19,700	55	M. Stenosis.	..	..	With acute nephritis.
19	25	...	....	19,600	..	M.	..	..	Pulmonary infarction; bloody pleurisy.
20	38	M.	3,648,000	19,300	45	M. Stenosis.	..	..	Albumin one-fourth per cent.
21	22	...	....	19,000	..	M.	..	..	With nephritis.
22	35	...	....	19,000	72	M.	..	..	Broken compensation.
23	35	...	....	18,000	..	M.			
24	9	...	....	18,000	60	M.	..	..	First day. Temp., 197°.
			4,160,000	23,000	55	....	..	..	Thirteenth day.
				30,000	65	....	..	..	Twenty-second day. Hydrothorax.
25	54	...	....	18,000	65	M.	..	..	Temp. 98°. Died.
26	22	...	....	17,900	80	M.			
27	30	...	....	17,100	65	M.	..	..	No fever.
28	40	...	....	16,800	65	M.	..	..	Temp., 101°+.
29	64	...	....	16,400	..	M.	..	..	Pulmonary infarction.
30	5	...	3,808,000	16,000	45	M.	..	..	Temp., 99.5°.
31	34	...	....	16,000	..	M.	A.	..	First day.
				11,000	..	....	..	..	Seventh day. Temp., 101°.
				21,000	68	....	..	..	Eighth day.
				14,200	..	....	..	..	Fourteenth day.
				9,400	..	....	..	..	Thirty-fifth day.
32	56	...	....	16,000	60	M.	A.		
33	47	...	....	15,400	..	M.	A.	..	Temp., 99-100°.
34	30	...	3,920,000	15,300	38	M.	A.	..	First day. Temp., 99°.
			3,840,000	8,600	43	....	..	..	Eleventh day.
				15,000	..	....	..	..	Temp., 97°.
35	38	...	....	14,100	65	M.	..	T.	
36	27	...	....	14,000	100	M.	A.	T.	First day.
				13,000	..	....	..	..	Third day.
37	49	...	....	14,000	..	M.	A.	..	With diffuse nephritis.
38	58	...	....	14,000	..	M.	..	..	Temp., 98°, with myocarditis.
39	34	...	....	13,400	..	M.	..	..	Temp., 98°, with nephritis.
40	58	...	3,814,000	13,400	50	M.	A.	..	Temp., 98°.
41	50	...	....	13,200	55	M.			
42	19	...	3,820,000	13,100	55	M.			
43	52	...	4,876,000	12,800	60	M.	A.	..	Temp. usually subnormal.

TABLE LV.—MITRAL VALVE DISEASES AND ITS COMPLICATIONS (*Continued*).

No.	Age.	Sex.	Red cells	White cells.	Per cent hæmoglobin.	Lesions.			Remarks.
						Mitral.	Aortic.	Tri-cuspid.	
44	21	...	....	12,800	..	M.	A.		
45	28	...	....	12,800	60	M.	A.		
46	52	...	....	12,500	80	M.	A.		
47	41	...	....	12,100	..	M.			
48	25	...	4,480,000	11.400	45	M.	A.	..	Temp., 98°.
49	46	...	4,500,000	11,200	40	M.	A.	..	With angina.
50	21	...	....	11,200	52	M.			
51	48	...	....	11,200	65	Double. M.			
52	68	...	....	11,000	..	M.	..	..	Temp., 98°.
53	34	...	....	11,000	..	M.			
54	33	...	....	10,700	65	M.	..	..	Temp., 98°.
55	45	...	....	10,600	..	M.	A.		
56	54	...	....	10,600	72	M.	..	..	Asthma.
57	43	...	....	10,200	77	M.	..	..	Broken compensation.
58	40	...	....	9,900	..	M.	A.	..	Temp. subnormal.
59	19	...	....	9,900	..	M.	..	..	Temp., 98°.
60	27	...	....	9,900	..	M.			
61	25	...	....	9,800	70	M.	A.		
62	40	...	....	9,600	..	M.			
63	28	...	....	9,600	..	M.	A.	..	Temp., 98°. Broken compensation.
64	20	...	....	9,500	70	M.	..	..	Temp., 100°.
65	39	...	....	9,400	65	Double. M.	..	..	Broken compensation.
66	54	...	....	9,400	..	M.	..	..	Broken compensation.
67	27	...	5,360,000	9,200	100	M.			
68	49	...	....	9,200	..	M.	A.		
69	33	...	....	9,000	72	M.			
70	27	...	....	9,000	..	....	..	..	December 14th.
			6,452,000	......	95	....	..	..	December 21st.
71	61	...	4,953,000	8,900	48	M.	..	..	Broken compensation. No autopsy.
72	49	...	....	8,800	60	M.	..	..	Temp., 98°.
73	46	...	....	8,800	..	M.			
74	..	...	....	8,600	..	M.	A.	..	Fever. Gonorrhœa (?).
75	46	...	....	8,500	..	M.	..	..	Temp., 97°.
76	40	...	....	8,400	..	M.	..	..	Temp., 96°.
77	40	...	....	8,200	..	M.	..	..	Temp., 98°.
78	38	...	....	8,000	..	M.	A.		
79	36	...	....	7,900	..	M.	..	..	Broken compensation. Temp., 97°.
80	41	...	....	7,900	..	M.			
81	50	...	....	7,800	..	Stenosis. M.	..	..	Temp., 97°.
82	44	...	4,040,000	7,500	55	M.			
83	49	...	....	7,300	..	Double. M.			
84	40	...	....	7,000	..	M.			
85	28	...	....	6,800	..	M.			
86	32	...	....	6,600	..	M.			
87	50	...	....	6,000	..	Double. M.			
88	30	...	1,600,000	6,000	10	M.	A.	..	First day. Polynuclear, 61.6; lymphocytes, 38; eosinophiles, 4; megaloblasts, 1; normoblasts, 8; reds pale, large, deformed.
			1,536,000	4,200	10	....	..	..	Seventh day. Polynuclear, 67; lymphocytes, 32; eosinophiles, 1; megaloblasts, 4; normoblasts, 7. Large oval forms.
			1,728,000	10,400	15	....	..	..	Fifteenth day.
			1,720,000	5,000	12½	....	..	..	Twentieth day. Polynuclear, 71; lymphocytes, 27; eosinophiles, 2; megaloblasts, 1.
			1,840,000	5,200	18	....	..	..	Twenty-seventh day.
89	59	...	....	6,000	..	M.	A.		
90	40	...	....	5,800	70	M.	..	..	Temp., 98°.
91	40	...	....	4,900	..	M.	A.		

MITRAL VALVE DISEASE AND ITS COMPLICATIONS.

Summary.

White cells.	Cases.
Between 2,000 and 6,000	7
" 6,000 " 8,000	41
" 8,000 " 10,000	46
" 10,000 " 12,000	42
" 12,000 " 14,000	38
" 14,000 " 16,000	28
" 16,000 " 18,000	23
" 18,000 " 20,000	19
" 20,000 " 22,000	8
" 22,000 " 24,000	9
" 24,000 " 30,000	8
" 30,000 or more	6
Total	270
Average	13,000 +

Total over 14,000 = 96 cases, or thirty-five per cent of all.

TABLE LVI.—AORTIC VALVE DISEASE.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	42	..	....	31,000	50	
2	25	..	....	30,600	80	
3	18	..	....	22,000	70	
4	26	..	....	20,400	95	Cerebral embolus.
5	43	..	....	19,900	80	
6	54	..	....	16,300	75	Chronic nephritis. Autopsy.
7	26	..	....	13,700	60	Chronic nephritis.
8	?	..	....	12,800	67	
9	52	..	....	12,000	60	First day. Temp. 101°.
				20,000	..	Third day. Temp. 102°.
				26,000	..	Sixth day. Temp. 102°.
				25,000	..	Eighth day. Temp. 101°.
				30,000	..	Fourteenth day. Temp. 101°.
				21,600	..	Twentieth day. Temp. 99.3°.
						Twenty-seventh day. Autopsy.
10	22	..	....	11,600	85	
11	40	..	....	9,700	70	
12	24	..	....	9,200	100	
13	38	..	....	8,600	85	
14	21	..	....	8,500	95	
15	56	..	....	7,800	..	Angina.
16	33	..	....	7,700	95	
17	57	..	....	7,600	68	
18	39	..	....	7,200	90	
19	74	..	....	7,200	65	
20	58	..	....	7,100	80	
21	?	..	....	7,000	68	
22	24	..	5,024,000	6,800	60	
23	39	..	....	6,600	75	
24	37	..	....	6,000	..	With chronic diffuse nephritis.
25	24	..	....	5,000		
26	78	..	....	3,200	..	Temp. 98°.
27	22	..	4,400,000	......	45	

The most important practical deduction from these data is that a blood count in a patient suffering from poorly compensated heart disease has no value in determining whether or not anæmia is present. The actual number of corpuscles in the body is not measured by the number contained in a drop of peripheral blood, since anæmia may be effectually masked by concentration or simulated by dilution.

This holds good equally for any condition involving *general* stasis and cyanosis either from embarrassment of the heart's action or otherwise (for instance, pneumonia in certain stage, emphysema, displacement of the heart by serous effusions, or tumors), or *local* stasis of the part from which blood is taken. Penzoldt[1] noted that in old hemiplegic cases the blood from the affected side contained more corpuscles than that from the sound side, and the writer has noticed the same thing in a variety of vasomotor affections involving local asphyxia.

ANEURISM.

As a rule I have found the blood entirely normal, but in the following case it might have thrown light on the diagnosis. A patient was recently admitted to the Massachusetts General Hospital with an acute affection of the chest, supposed to be pneumonia in spite of the slightness of the fever and the irregularity of the physical signs. At autopsy a ruptured aortic aneurism was found. The blood count had showed 3,324,000 red cells, 20,800 white, and 33 per cent hæmoglobin. The low percentage of hæmoglobin and red cells was really inconsistent with an acute pneumonia in a man previously well, and might have hinted strongly toward the correct diagnosis had attention been directed more carefully to the blood. After gelatin injections, leucocytosis always appears.

DISEASES OF THE KIDNEYS.

Many factors other than the disease itself may influence the blood of nephritic cases. For instance, in scarlatinal nephritis the long-standing leucocytosis is probably due largely to the scarlatinal poison, rather than to the nephritis. The occurrence of large quantities of blood in the urine has the same influence as any other hemorrhage upon the blood.

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[1] Berliner klin. Woch., 1881, p. 457.

Œdema as such has apparently very little effect upon the blood, but the *loss of albumin* in the urine tells both on the corpuscles and on the serum, thinning both with consequent lowering of the specific gravity of the blood.

ACUTE NEPHRITIS.

1. *Red Cells and Hæmoglobin.*

Whether largely from the loss of blood from the kidneys or from other causes, the red cells are often much diminished, but the hæmoglobin suffers still more.

Laache reports an average loss of nineteen per cent of the red cells and twenty-six per cent of their coloring matter.

Hayem found no considerable loss of red cells unless the urine was hemorrhagic. The following cases illustrate his results:

Case I.—Acute nephritis, ending in recovery.

	Red cells.
March 17th, 1882	3,069,000
March 31st, 1882	2,759,000
April 7th, 1882	2,821,000
May 1st, 1882, albuminuria ceased.	
May 17th, 1882	3,038,000
May 31st, 1882	3,689,000

Case II.—Acute (puerperal) nephritis; recovery.

	Red cells.
April 6th, 1881	2,945,000
" 9th, 1881	2,976,000
" 12th, 1881, no albumin in urine.	
" 13th, 1881	3,137,500
" 20th, 1888	3,310,000

Case III.—Nephritis (chronic?) with hæmaturia.

Red cells 2,821,000

(It should be noted that Hayem's counts are low on the average, and the instrument used by him was not very reliable.)

Grawitz in acute nephritis records 3,400,000 red cells at the beginning of the third week and 3,100,000 ten days later.

Koblank[1] counted 5,168,700 in a case of acute nephritis with œdema.

Sadler (*loc. cit.*) in six cases of acute nephritis found in two

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[1] Inaug.-Dissert., Berlin, 1889.

,000 and 2,262,000 red cells; in the other four practically al counts.

eraccini[1] found no appreciable anæmia.

TABLE LVII.—ACUTE NEPHRITIS.

	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	33	..	3,568,000	50,000	37	Uræmia. Septic endometritis.
	mos.	..	....	36,000	..	Parenchymatous.
		..	....	31,000	75	
		..	5,020,000	27,000	70	
		..	....	23,000	65	
	6	F.	... ...	22,000	..	Temperature 102.5°.
				14,000	..	Sixth day.
				11,900	..	Ninth day temperature falling.
				12,200	..	Nineteenth day.
	33	..	....	21,200	65	Uræmia. July 13th.
				44,800	..	Lobar pneumonia. July 19th.
				32,000	..	July 22d.
				31,000	..	July 28th.
				21,000	..	August 2d.
				25,000	..	August 5th.
				21,000	..	August 7th.
				21,000	..	August 11th.
				29,000	..	August 13th.
				31,000	..	August 16th.
				13,000	..	August 21st.
				11,000	..	August 23d.
				9,300	..	August 25th.
8	35	..	....	21,000	70	
9	46	..	....	17,200	90	
10	18	..	....	17,000	85	
11	32	..	....	17,000	90	Uræmia. August 4th.
				6,500	..	August 29th.
12	54	..	... .	16,850	70	
13	14	..	....	15,200	75	
14	14	..	....	15,100	70	December 13th.
				30,100	..	December 18th.
				28,600	..	December 19th.
				22,400	..	December 20th.
15	24	..	4,020,000	14,000	60	
16	11	F.	4,068,000	14,000	52	
17	30	..	....	13,700	90	
18	45	M.	3,532,000	13,200	43	
19	42	..	4,304,000	13,000	36	
20	40	..	4,880,000	12,700	65	
21	40	..	....	12,600	75	
22	20	..	....	12,500	65	Uræmia.
23	13	F.	....	12,000		
24	11	..	....	11,800	70	
25	23	M.	....	11,700	50	
26	25	..	....	11,600	75	
27	35	..	....	11,500	85	
28	24	F.	....	11,100	85	

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[1] Pieraccini: "La Morfologia del Sangue nelle Nefriti," Florence, 1901.

TABLE LVII.—ACUTE NEPHRITIS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
29	..	..	5,228,000	10,800	50	
30	25	..	....	10,400	60	
31	26	..	....	10,400	70	
32	33	M.	3,904,000	9,800	50	Purpura also.
33	29	..	....	9,300	85	
34	32	..	....	8,700	85	
35	22	M.	4,800,000	8,800	48	
36	38	..	....	8,000	75	
37	22	M.	....	7,600	60	
38	44	F.	....	7,500	65	
39	37	M.	....	6,800	78	
40	13	..	....	6,800	85	
41	25	..	4,080,000	6,600	40	Parenchymatous.
42	55	..	....	6,200		
43	20	..	....	6,200	..	Parenchymatous.
44	20	M.	5,000,000	6,000	58	Acute parenchymatous.
45	54	..	....	6,000	75	
46	33	..	3,568,000	5,900	60	October 20th.
			3,584,000	6,800	60	November 3d.
47	22	F.	4,044,000	5,400		
				5,100	..	Acute parenchymatous.
48	20	..	4,090,000	5,100	55	
49	39	..	3,752,000	......	65	
50	40	..	....	4,600	77	

In none of the few cases examined at the Massachusetts General Hospital were the red cells much diminished, but in two cases the hæmoglobin was low, the color index being 0.62 in one and 0.61 in the other.

The blood plates are much increased (Hayem) and fibrin is slightly increased.

2. *White Cells.*

Leucocytosis is usually stated to be the rule, lasting often for weeks at a time and gradually diminishing in convalescence.

Hayem gives counts of 14,973, 12,400, 15,000, and 13,000.

Koblank (*loc. cit.*) and Grawitz each in a single case found *normal* counts (7,300 and 5,600).

Sadler found an increase in only one of his six cases, and then the highest point reached was 13,312.

Of the fifty cases of Table LVII., leucocytosis was present in twenty-one, in one of which it was followed for three weeks and still persisted; but it is my own belief that the leucocytosis of acute

due either to complications, to loss of blood by the kid-
ræmia. When these conditions have been absent I have
any leucocytosis. This agrees with Pieraccini's results.

RONIC DIFFUSE AND CHRONIC PARENCHYMATOUS NEPHRITIS.

Red Cells.

In advanced stages the counts may run very low, but more often
s chiefly the hæmoglobin that suffers. Hayem gives the follow-
figures:

CASE I.—Chronic parenchymatous nephritis.

	Red cells.	Per cent Hb.
June 20th	4,309,000	43
July 4th	4,216,000	44
October 18th	2,945,000	34

CASE II.—Same diagnosis.

	Red cells.	Per cent Hb.
March 6th	2,619,500	36
" 8th	2,836,500	36
" 23d	2,464,500	27

Koblank (*loc. cit.*) in the same disease found 3,291,700 red cells in a single case with much œdema.

Reinert found 4,050,000 with 50 per cent of hæmoglobin and 3,604,000 with 62 per cent of hæmoglobin.

Sadler.

	Red cells.
Case 1	4,120,000
" 2	2,405,000—November 19th. 1,110,000—January 14th. 1,500,000—January 17th.
" 3	4,300,000
" 4	4,300,000
" 5	3,737,500—June 28th. 3,593,700—July 3d. 2,187,500—August 15th.
" 6	3,200,000—July 7th. 3,257,000—July 22d. 3,137,000—August 21st.

Grawitz in an acute exacerbation of a chronic parenchymatous nephritis found 1,928,000 red cells. Da Costa in a series of 15 cases found the red cells from 2,270,000 to 5,520,000—average 3,971,000; the hæmoglobin from 30 to 82—average 57 per cent; leucocytes from 4,000 to 16,000—average 8,600.

The Massachusetts General Hospital cases show a considerable anæmia in forty-one out of the sixty-four, or two-thirds of the series. Great concentration or cardiac weakness is probably the cause of the very high counts in certain cases. The majority of cases are not far from normal so far as the number of red cells goes, and the hæmoglobin is also very little diminished.

CHRONIC NEPHRITIS.

Red cells.	Cases.
Between 1,000,000 and 2,000,000	8
" 2,000,000 " 3,000,000	12
" 3,000,000 " 4,000,000	26
" 4,000,000 " 5,000,000	14
" 5,000,000 " 6,000,000	6
" 6,000,000 " 7,000,000	8
Color index averages about 0.7.	64

White Cells.

Hayem records 25,000, 19,000, 13,000, 10,000, and 6,000, and concludes that the counts vary much not only in different cases, but in the same case at short intervals.

Koblank found 14,700 in a single case.

Sadler in one case found 6,300 in November and 16,000 in the following January; 12,000 in another case; 8,800, 7,700, and 1,916 in others.

TABLE LVIII., A.—COUNTS IN CHRONIC NEPHRITIS WITH URÆMIA.

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
32	F.	....	44,000	..	Eclampsia.
35	..	....	25,000	..	Coma first day.
			9,000	..	Clear twelfth day.
29	F.	....	22,600		
21	..	4,080,000	20,400		
29	.	....	18,900	80	Temperature, 102.5°.
29	M.	....	18,650	..	Polynuclear, 83%.
35	F.	....	18,600	..	Coma five weeks after miscarriage.
35	..	....	18,000	..	November 21st, arterio-sclerosis.
			15,800	..	November 23d.
		4,184,000	18,100	60	December 2d.
		2,320,000	16,800	18	January 4th.
18	..	....	17,800	81	

VIII., A.—COUNTS IN CHRONIC NEPHRITIS WITH URÆMIA (*Continued*).

	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	..	5,236,000	17,450	52	Eclampsia.
	F.	....	16,800		
	..	....	16,300	..	Chronic diffuse.
	..	4,650,000	16,300	58	Polynuclear, 86.7%. Lymphocytes, 13.3. No nucleated reds or deformity.
	..	3,604,000	16,200	50	Chronic diffuse.
	F.	....	15,800	..	Differential count normal.
	..	....	15,800	..	Chronic diffuse. Eclampsia.
	..	....	15,000		
			13,200		
	M.	....	15,000		
	M.	....	15,000		
	..	....	14,300	70	Chronic diffuse. Died in one month.
	M.	....	14,200		
	F.	....	13,800		
	M.	....	13,400		
	..	2,360,000	12,800	44	Polynuclear, 77%. Eosinophiles = 0.
	M.	....	12,500		
	M.	....	12,400		
	..	....	12,400	60	
	F.	....	12,300		
19	..	3,104,000	12,200	35	Chronic diffuse.
59	M.	....	12,100		
9	..	....	11,900	..	Interstitial. Asthma.
63		....	11,400		
44	M.	....	11,300		
81	M.	....	11,200		
48	..	2,448,000	9,800	35	
44	..	....	8,400	100	
81	..	2,500,000	7,500	30	
45	F.	....	6,600		
84	F.	....	4,600		
80	M.	....	4,200		

CHRONIC NEPHRITIS WITH URÆMIA.

Summary.

White cells.	Cases.
Between 2,000 and 6,000	6
" 6,000 " 8,000	9
" 8,000 " 10,000	11
" 10,000 " 12,000	13
" 12,000 " 14,000	15
" 14,000 " 16,000	12
" 16,000 " 18,000	9
" 18,000 " 20,000	8
" 20,000 or more	11
Total	94
Average	15,100 +

TABLE LVIII., B.—CHRONIC DIFFUSE NEPHRITIS. NO URÆMIA.

Age.	Sex.	White cells.	Age.	Sex.	White cells.	Age.	Sex.	White cells.
26	..	24,700	17	M.	10,400	28	M.	7,600
55	..	23,200	50	..	10,300	25	M.	7,600
21	..	19,000	43	F.	10,300	17	M.	7,500
55	..	18,500	20	..	10,200	55	M.	7,400
51	..	18,000	28	..	10,100	34	M.	7,400
45	M.	16,300	52	..	10,000	50	F.	7,300
11	..	16,000	60	..	10,000	26	..	7,300
66	..	15,800	20	F.	10,000	28	M.	7,000
43	M.	14,500	52	F.	9,800	42	..	7,000
19	..	14,300	30	..	9,500	41	M.	6,800
56	F.	14,000	25	..	9,000	8	M.	6,800
66	M.	14,000	24	F.	9,000	8	M.	6,500
47	..	13,100	36	..	8,800	39	M.	6,500
27	M.	13,000	54	..	8,700	7	M.	6,400
11	M.	13,000	45	..	8,300 April 5th	20	F.	6,250
38	..	12,800 April 4th			13,000	41	M.	5,500
		13,900 April 6th			April 9th.	42	..	5,500
		28,650	30	M.	8,300	30	F.	5,200
		April 9th, died.	27	F.	8,300	27	M.	5,100
16	F.	12,700	58	..	8,200	30	M.	5,000
48	..	11,200	16	..	8,100	58	M.	4,800
25	M.	11,200	56	..	8,100	30	M.	4,500
10	F.	11,000	33	M.	7,900	41	M.	3,000
47	F.	10,800	14	M.	7,750	25	..	1,400
56	M.	10,700	15	F.	7,700			

The same wide range is seen in Table LVIII., A and B, in which I have divided the uræmic and the non-uræmic cases into separate tables. It will be seen from these that fifty-five out of ninety-four uræmic cases showed leucocytosis, while sixty-one out of ninety-two non-uræmic cases showed no leucocytosis. It is impossible to suppose that this is mere coincidence.

TABLE LIX.—CHRONIC DIFFUSE NEPHRITIS. NO URÆMIA.

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
20	..	3,492,000	39,000	42	With bronchitis.
26	..	3,500,000	26,300	50	With acute articular rheumatism.
36	..	2,560,000	16,100	35	April 14th.
			12,400	20	April 30th.
			8,900	..	May 1st.
37	..	3,144,000	16,000	40	
11	..	3,660,000	15,600	52	
33	..	3,568,000	14,600	45	
22	..	4,272,000	14,400	45	Sub-acute.
19	..	5,864,000	14,300	65	Amyloid liver and spleen. February 12th.

TABLE LIX.—CHRONIC DIFFUSE NEPHRITIS; NO URÆMIA (*Continued*).

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
		6,092,000	13,700	..	From ear.
		5,740,000	13,700	..	From finger.
24	..	3,824,000	11,400	55	
		4,268,000	13,600		
16	..	3,724,000	11,300	45	
35	..	3,164,000	10,600	50	Tertiary syphilis.
42	..	4,228,000	10,100	65	Œdema.
19	..	3,776,000	10,000	56	Cardiac hypertrophy.
28	..	4,560,000	10,000	45	
47	..	4,450,000	9,800	50	
21	..	4,080,000	8,600	70	
42	..	3,416,000	7,000	55	
55	..	4,360,000	6,300	50	Ascites.
24	..	4,800,000	5,700	65	
26	..	1,468,000	3,800	23	Polynuclear, 70%; lymphocytes, 23%; large lymphocytes, 4.4%; eosinophiles, 2.6%; reds, megaloblasts, 3; normoblasts, 2; microblasts, 1. Considerable variation in size; many oval forms; considerable poikilocytosis.
		1,136,000	......	19	Polynuclears, 71.8%; lymphocytes, 24.2%; large lymphocytes, 2.2%; eosinophiles, 1.2%; myelocytes, 6; megaloblasts, 6; normoblasts, 3. November 5th.
		1,752,000	......	22	Polynuclears, 69.4%; lymphocytes, 25.2%; large lymphocytes, 3.8%; eosinophiles, 1.6%; megaloblasts, 4; normoblasts, 2. November 13th.
		2,248,000	......	30	Polynuclears, 65.4%; lymphocytes, 28%; large lymphocytes, 3%; eosinophiles, 3.4%; basophiles, 2; megaloblasts, 1; normoblasts, 0. November 20th.
		2,540,000	......	48	Polynuclears, 70.2%; lymphocytes, 23%; large lymphocytes, 2.6%; eosinophiles, 3.4%; basophiles, .8%. Red variation in size and shape less marked. Megaloblasts, 1. November 27th.
		3,392,000	......	60	December 6th.
		3,580,000	5,800	65	Polynuclears, 79%; lymphocytes, 17.6%; large lymphocytes, 1.8%; eosinophiles, 1.6%. Reds stain well; slight poikilocytosis and variation in size; no nucleated reds.
36	...	5,060,000	......	75	Hemorrhagic nephritis.

CHRONIC DIFFUSE NEPHRITIS; NO URÆMIA.

White cells.	Cases.
Between 2,000 and 6,000	**4**
" 6,000 " 8,000	**12**
" 8,000 " 10,000	**18**
" 10,000 " 12,000	**27**
" 12,000 " 14,000	**11**

Between 14,000 and 16,000	9
" 16,000 " 18,000	5
" 20,000 + or more	6
Total	92
Average	11,600 +

CHRONIC INTERSTITIAL NEPHRITIS.

Hayem found the fibrin more increased in this form of nephritis than in any other, and the anæmia less pronounced.

Grawitz distinguishes two stages:

I. As long as the heart is strong enough to overcome the increased resistance at the periphery and the disturbances of circulation are not marked, the blood is normal.

II. When compensatory hypertrophy is no longer sufficient to do the work of forcing the blood through the system, the usual effects of failing compensation (see Heart Disease, page 353) appear (dilution and subsequent concentration of the blood).

The *white cells* are normal.

Pieraccini (*loc. cit.*) has recently studied with care seventeen cases of nephritis of various types, paying especial attention to the differential count of leucocytes. He concludes (page 282) that: "Toxæmia of renal origin, occurring in any variety of nephritis, diminishes the number of circulating eosinophiles in proportion to the degree of the toxæmia. In the severest cases the eosinophiles altogether disappear from the circulation. . . . With the remission of toxic symptoms the eosinophiles tend to return to normal or to rise above normal." The disappearance of eosinophiles from the blood of a case of nephritis is therefore, he says, a bad prognostic sign. This is of special importance in the nephritis of pregnancy.

In conditions resembling those of uræmia—*e.g.*, hysterical, epileptic, or syphilitic convulsions, coma from alcoholism, apoplexy or following epilepsy, cardiac asthma or cardiac œdema—Pieraccini finds the eosinophilic cells undiminished. [He does not refer to the type of convulsions occurring in dementia paralytica and other types of insanity in some of which Capps and Burrows found marked diminution or absence of eosinophiles (see page 389), but it is very possible that these convulsions were also of toxic, if not of uræmic origin.]

Pieraccini considers the percentage of eosinophiles a valuable datum in the diagnosis between bronchial asthma and renal asthma. In the latter there is a diminution, in the former an increase of eosinophiles. Between a "cardio-renal" and a "reno-cardial" dropsy

s the presence of eosinophiles in normal or increased per-
ne mean that the heart and not the kidney is chiefly to blame.
reappearance of eosinophiles, however, does not seem to him
the prognosis as much in uræmic states as it appears to in
ous liseases (Türck). Especially in chronic uræmia the sys-
een to become so adjusted to its burden that the eosinophiles
pear and remain in the circulation despite decided symp-
of systemic poisoning (*loc. cit.*, p. 193).

r respects Pieraccini finds no abnormalities in the blood
t nephritis. The number and quality of erythrocytes, leu-
s, and platelets are normal. Rouleaux formation, coagulation,
the size and staining reaction of the corpuscles are also normal.

TABLE LX.—CHRONIC INTERSTITIAL NEPHRITIS.

o.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	29	....	23,700	65	
	26	....	19,700	70	Death.
	39	6,040,300	19,000	80	Coma; moribund.
	31	....	17,200	70	March 25th.
			15,400	65	March 30th.
	56	....	16,200	95	
6	..	4,548,000	15,000	50	
7	58	....	14,500	75	Uræmia.
8	35	....	14,400	85	Uræmia.
9	40	....	14,100	60	Chronic gastritis.
10	23	....	13,600	65	Uræmia. Autopsy.
11	36	....	13,600	72	Uræmia.
12	50	....	12,800	65	Death.
13	47	....	12,600	70	Retinitis.
14	26	....	12,400	90	
15	51	....	12,300	80	Mitral sufficiency.
16	50	....	12,200	90	Mitral sufficiency.
17	..	4,240,000	12,000	67	
18	22	....	11,600	65	
19	64	....	11,200	75	
20	22	5,020,000	11,100	50	
21	23	....	10,800		
22	40	3,150,000	9,800	80	
23	46	....	9,700	..	Uræmia; moribund.
24	69	....	8,500	87	
25	34	3,536,000	8,300	57	
26	47	....	8,200	80	
27	60	....	7,800	95	Cerebral hemorrhage.
28	46	....	7,300		
29	52	....	6,800	80	Uræmia.
30	52	....	6,800	65	Uræmia.
31	20	4,088,000	6,000	52	
32	32	....	6,000	65	
33	60	....	5,900		
34	36	....	5,400	60	

PYELONEPHRITIS.

Table LXI. speaks for itself. The *anæmia* is often severe and leucocytosis is the rule in my experience, but Pieraccini reports (*loc. cit.*, p. 252) four cases of "open pyelonephritis" with or without cystitis, none of which showed any leucocytosis nor any change in the percentage of the different leucocytes.

Table LXI.—Pyelonephritis.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	24	F.	3,056,000	21,200	41	March 10th. Uræmia.
			2,976,000	15,200	38	March 13th.
			2,696,000	18,800	33	March 27th.
			3,272,000	25,200	33	April 14th.
2	26	F.	4,200,000	16,800	..	Perinephritic abscess too.
3	33	M.	4,536,000	15,550	36	Cystitis also.
4	26	F.	2,356,000	7,280	65	Cystitis also.
5	40	..	....	6,800	..	Pyelitis.

Table LXII.—Cystic Kidney.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	55	M.	3,664,000	4,400	..	Polynuclear cells, 72 per cent. Supposed cancer. Enormous firm tumor on each side. Autopsy.

The cases recorded in Table LX. are probably not inconsistent with these rules. Of the seven cases with leucocytosis three were uræmic, and in a fourth the influence of digestion is seen. The hæmoglobin is lower than we should expect from Grawitz's account.

Uræmia, it would appear from these tables, may cause leucocytosis, or at any rate is not infrequently associated with it. Aside from uræmia and hemorrhage, nephritis probably does not cause leucocytosis.

STONE IN THE KIDNEY.

(See Table LXIII.) The state of the blood depends on the amount of ulceration caused by the stone; when this is considerable we have leucocytosis.

TABLE LXIII.—STONE IN THE KIDNEY.

ge.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
.	..	....	22,800	85	Tender in loin.
			16,200		
1	..	....	16,500	..	August 10th.
			10,800	..	August 12th. Pain gone.
	..	....	15,600	80	
	M.	....	15,200	..	Much pus in urine.
	M.	4,350,000	14,750	78	
	..	....	12,900	73	
	..	....	10,200		
	F.	4,160,000	9,000	65	
	M.	....	8,990		
	..	....	8,600	85	
	M.	5,680,000	8,000		
	..	....	7,800	85	Hæmaturia.
	M.	3,048,000	7,500	30	
15	M.	....	7,500	95	
1	M.	....	6,000	95	Uric-acid stone passed.
	..	....	5,300	88	
	..	....	5,300	70	
	M.	....	4,980	85	
..	..	4,340,000	3,000	..	Much pus in urine.
		6,100,000	16,500	..	Two weeks later.

Diagnostic Value.

Cancer would also cause leucocytosis, but would not increase fibrin as a rule, while most cases of stone with ulceration do increase fibrin.

FLOATING KIDNEY.

The blood is normal. This fact has some diagnostic value; for example, when we confound appendicitis with floating kidney, as has been done (see page 260). The presence of leucocytosis excludes the latter and favors the former. Most tumors or abscesses with which a floating kidney might be confused could be distinguished by the same criterion.

TABLE LXIV.—FLOATING KIDNEY.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	47	..	4,650,000	23,000	45	March 28th. Peritoneal inflammation.
				17,400	..	April 4th.
				21,300	..	April 9th.
				21,800	..	April 15th. Diff. count 300. Polynuclear, 87 per cent; small lymphocytes, 7; large lymphocytes, 5.5; eosinophiles, .5; reds average size; very few poikilocytes.

TABLE LXIV.—FLOATING KIDNEY (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
2	65	..	4,432,000	11,800	65	Double.
3	24	..	....	11,200	70	
4	37	F.	5,056,000	9,200	75	
5	41	F.	4,684,000	9,000	75	
6	24	F.	....	8,100		
7	67	F.	....	8,000	65	
8	23	F.	5,400,000	6,000	69	
9	43	F.	4,700,000	2,400	76	
10	38	F.	....	....	75	Aneurism of arch also.
11	24	F.	....	....	80	
12	38	F.	4,416,000	5,800	67	
13	24	F.	....	7,600	80	

A large number of similar counts might be quoted.

HYDRONEPHROSIS.

TABLE LXV.—HYDRONEPHROSIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	52	..	4,016,000	16,400	75	March 7th.
				10,800	..	March 12th.
2	4	..	5,496,000	14,300	60	
				28,600	..	Operation. Congenital.
3	24	..	5,140,000	9,200	80	Intermittent.
4	35	.	....	6,500	85	

PYONEPHROSIS.

CASE I.—Female, 36; leucocytes, 16,200, of which 85 per cent are neutrophiles. Half a pint of pus found at operation.

CASE II.—July 25th—Red cells, 3,856,000; white cells, 9,800; hæmoglobin, 45 per cent. July 9th—Red cells, 3,450,000; white cells, 9,000; hæmoglobin, 55 per cent. August 3d—White cells, 6,650. August 6th—Operation. Pint of foul pus. Death.

DISEASES OF THE LUNGS.

BRONCHITIS.

"Acute catarrhal and chronic purulent bronchitis have relatively little leucocytosis in most cases" (v. Limbeck).

Except for this and a few other passing references, there is hardly anything in literature on the blood in bronchitis, so that I shall be forced to base my statements chiefly on the few counts recorded at the Massachusetts General Hospital.

ACUTE BRONCHITIS.

Aside from "capillary bronchitis," cases are not infrequently seen in which the signs are simply those of general bronchitis of the finer tubes, yet the symptoms are much more like pneumonia. Whatever may be the real conditions in the lungs of such patients, their blood is not infrequently exactly like that of pneumonia and does not help at all in the differential diagnosis between the two diseases (see Cases 1 and 2, Table LXVI.).

TABLE LXVI.—ACUTE BRONCHITIS.

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
75	..	5,808,000	45,000	58	
			26,400	..	Fourth day.
			68,800	..	Eleventh day; died.
70	F.	4,420,000	41,000	70	
56	F.	4,800,000	26,000	65	Temperature, 103°.
6	..	....	26,000	..	Whooping cough.
28	..	....	25,900	67	Temperature, 101°.
			17,100	..	Fourth day; well.
32	..	....	25,750	..	Subacute; temperature, 99°.
34	..	....	23,500	80	With enteritis; temperature, 103°.
22	M.	....	23,450	67	Temperature, 101°.
21	..	....	22,200	..	Temperature, 101°.
7	..	....	21,200	..	Temperature, 103°.
58	..	....	20,400		
44	..	5,660,000	20,100	58	Temperature, 103°; asthma.
31	..	....	19,100	..	Temperature, 100°.
3	..	....	19,000	..	Temperature, 99.5°.
36	..	....	19,000	..	Temperature, 98°.
50	..	....	17,200	62	Subacute.
42	..	....	17,000	..	First day; temperature, 100°.
			15,000	..	Four days later, temperature, 98°.
38	..	....	15,100	..	Temperature, 103°.
41	F.	4,192,000	15,000	65	November 5th.
			11,300	..	November 16th.
			17,600	..	November 25th.
55	..	....	15,000	..	Subacute; temperature, 100°.
26	M.	....	14,200	70	Temperature, 101.5°.
22	..	....	13,800	60	Temperature, 102°.
			16,300	..	Third day.
			16,400	..	Sixth day.
55	..	....	13,000	..	Temperature, 100°.
5	..	....	13,000	..	Temperature, 102.5°.
			12,600	..	Third day; temperature, 101°
			11,300	..	Sixth day; temperature, 100°.
			6,600	..	Eleventh day; temperature, 98°.
23	..	....	12,600	..	Temperature, 101.5°
30	..	....	12,000	65	Temperature, 102°.
28	F.	6,196,000	12,000	..	

TABLE LXVI.—ACUTE BRONCHITIS (*Continued*).

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
46	M.	....	11,800	..	Temperature, 104°.
13	..	....	10,800	..	Temperature, 102°.
20	M.	....	10,600	65	Temperature, 104°.
40	M.	....	10,300	..	Temperature, 101°.
31	..	....	10,200	..	Temperature, 102°.
69	..	....	9,400	..	Temperature, 101°.
42	M.	....	9,300		
50	F.	5,260,000	8,000	72	
50	M.	5,952,000	7,900	50	
38	..	....	7,800	..	Temperature, 99°.
48	..	....	7,800	..	Temperature, 102°.
25	..	....	7,200	..	Temperature, 100°.
52	M.	....	7,000	70	
25	M.	....	7,000	74	Temperature, 103°.
56	F.	....	6,800		
36	M.	4,392,000	6,000	72	October 31st.
			8,600	..	November 3d.
43	..	....	5,900	..	Temperature, 100°.
29	M.	....	4,000	80	Temperature, 102°.

ACUTE AND SUBACUTE BRONCHITIS.

	White cells.			Cases.
Between	2,000	and	6,000	13
"	6,000	"	8,000	31
"	8,000	"	10,000	18
"	10,000	"	12,000	22
"	12,000	"	14,000	17
"	14,000	"	16,000	15
"	16,000	"	18,000	10
"	18,000	"	20,000	13
"	20,000	"	22,000	8
"	22,000	"	24,000	7
"	24,000	"	26,000	7
"	26,000	"	45,000	7
Total				168
Average				12,800 +

TABLE LXVII.—CHRONIC BRONCHITIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	51	..	....	38,000		
2	32	..	....	30,400	80	
3	24	..	....	29,500		
4	Adult	M.	3,680,000	18,500	63	
5	52	..	....	18,400	90	

able LXVII.—Chronic Bronchitis (*Continued*).

ge.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	..	....	17,100	70	
	..	....	16,600	70	
	..	....	16,400	..	With emphysema.
	..	....	15,400	80	
	M.	....	15,000	..	Chronic febrile, with laryngitis. Recovery.
64	..	....	15,000	..	Temp. 98.6°.
32	..	....	14,300	..	Temp. 100°; with asthma.
55	..	....	12,900	..	Fibrinous.
58	..	....	12,400	85	
43	..	....	11,000	..	Temp. 98°; chronic with emphysema.
0	..	....	10,500		
6	..	....	10,100	80	
4	..	....	8,900	..	Temp. 98°.
27	F.	5,384,000	8,800	73	Constipation; neurasthenia; two weeks afebrile.
61	M.	4,300,000	8,000	63	Five months.
	F.	....	7,925	78	
	M.	....	7,792	..	Keratitis, conjunctivitis. No symptoms.
26	F.	4,700,000	6,700	70	Asthma.
45	..	....	6,700	62	
29	F.	4,100,000	5,500	61	Empyema of the antrum.
20	M.	....	5,062	..	One month.

In the majority of acute cases, however, the blood shows no changes unless concentration due to cyanosis be present.

In chronic cases (Table LXVII.) leucocytosis is uncommon; more so, I think, than the table represents. If more counts were added, nearly all, I think, would be normal.

The red cells and hæmoglobin show no changes to speak of in either acute or chronic cases.

The blood has no diagnostic value so far as I know, except that when pneumonia is in question a normal count of white cells speaks against it and in favor of bronchitis. If emphysema is also present, it sometimes produces a condition of the blood different from that in simple bronchitis.

EMPHYSEMA AND ASTHMA.

Grawitz reports an increase in the number of red cells in *emphysema*, which he believes to be due to cyanosis, and this covers up the really anæmic condition of the blood of many patients. Practically the same conditions are present as in the cyanosis of heart disease (see page 353) and the concentration of the blood is brought about in the same way. Leichtenstern[1] noticed a diminution in hæmoglobin at the time when the heart first fails, due probably to the diminished blood pressure which allows the lymph from neighboring tissues to flow into the vessels and dilute the blood.

In both asthma and emphysema it has been noted by Müller,[2] Gollasch,[3] Gabritschewsky[4] and others that *eosinophiles* are very numerous in the sputum, and Fink[2] also noted an increase of the same cells in the blood, running as high as 14.6 per cent instead of the normal one to two per cent. This increase is present only at the time of the paroxysm and for a short time before and after it. Von Noorden found in one case 25 per cent of eosinophiles during an attack, and a few days later could discover but one eosinophile in twelve cover slips. In another case, after five attacks on successive days, the eosinophiles were 33 per cent. Billings[5] reports the following counts:

	January 26th.	February 4th.	February 11th.
Red cells.	3,911,000	4,221,000	4,630,000
White cells	8,300	7,500	7,600
Hæmoglobin	68.0 per cent.	75 per cent.	86 per cent.
Polymorphonuclear cells	36.0 per cent.		
Lymphocytes (small)	5.0 per cent.		
Lymphocytes (large)	5.2 per cent.		
Eosinophiles	53.6! per cent.	38.2 per cent.	33.9 per cent.
	Few normoblasts.	... .	No nucleated red cells.

Their presence in increased numbers before a paroxysm is said to make it possible to predict its coming (v. Noorden, Schwerskewski). Coler reports a case of asthma with leucocytosis of 52,000, 25 per cent of which was made up of eosinophiles. The case was complicated with extensive purpura, painful muscles, and extreme cyanosis, but microscopic examination of the affected muscles showed no trichinæ.

Wolff[6] followed a case for over a year and found the eosinophiles always over ten per cent, although during six months of this time there were no paroxysms. He has noted similar conditions in two cases of hay fever.

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[1] "Ueber das Hb-Gehalt des Blutes," etc., Leipsic, 1878.

[2] Ref. in Fink, "Beiträge z. Kennt. des Eiters," Dissert., Bonn, 1890.

[3] Fortschritte der Med., 1889.

[4] Arch. f. exp. Path. und Pharm., 1890, p. 83.

[5] New York Med. Journal, May 22d, 1897.

[6] Wolff: Ziegler's Beiträge, vol. xxviii.

I have watched one subacute case without well-marked paroxysms or periods of perfect health. The blood was frequently examined and showed always a slight leucocytosis with eleven to fifteen per cent of eosinophiles. As this applies only to pure *bronchial asthma* and not to cases secondary to disease of the heart or kidney, Schreiber states that we are enabled to distinguish bronchial from cardiac or renal asthma by the increase of eosinophiles in the blood and sputa in bronchial cases, which does not occur in asthma due to cardiac and renal trouble. Pieraccini confirms this. Other records are (Gabritschewsky):

Case I.—	White cells	8,200
	Eosinophiles	10.08 per cent.
Case II.—	White cells	6,800
	Eosinophiles	22.4 per cent.
	Polynuclears	35 "

TABLE LXIX.—ASTHMA.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	55	..	....	39,000	90	Bronchial asthma; bronchopneumonia.
						February 2d. Diff. count 200 cells: Polynuclear, 88 per cent; small lymphocytes, 3; large lymphocytes, 9; eosinophiles, 0.
				55,000	..	February 5th.
				33,000	..	February 7th
				30,000	..	February 9th.
				20,000	..	February 12th.
				21,000	..	February 14th.
				18,000	..	February 17th.
				19,000	..	February 26th.
2	26	M.	....	32,500	..	Fifth. Temp. 100°. Bronchitis and emphysema.
				19,200	..	Seventh. Temperature normal.
3	45	..	....	32,000	85	March 16th. Emphysema; pneumococcus; bronchitis.
				28,000	..	March 19th.
				30,000	..	March 22d.
				28,000	..	March 30th.
4	33	..	....	31,500	85	July 17th; influenza.
				39,000	..	July 23d.
5	50	..	....	28,000	75	Emphysema; bronchitis; mitral insufficiency.

TABLE LXIX.—ASTHMA (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
6	31	..	....	21,000	95	Bronchial with unresolved pneumonia. Diff. count 500 cells: Polynuclear, 71.4 per cent; lymphocytes, 24.8; eosinophiles, 3.8.
7	29	..	....	20,000	67	Bronchial.
8	50	F.	....	19,800	50	Typical bronchial asthma during paroxysm.
9	29	..	....	18,600	85	Diff. count: Polynuclear, 57.3 per cent; lymphocytes, 28.9; eosinophiles, 13.8.
10	55	..	....	16,400	90	
11	78	..	....	16,000	65	February 14th.
				13,800	..	February 16th. Death.
12	27	..	....	15,400	90	Mitral insufficiency.
13	32	..	....	14,300	72	Bronchial.
14	44	..	....	14,200	95	Nasal; chronic ethmoiditis.
15	36	..	....	13,800	85	Bronchial.
16	38	..	....	13,600	80	
17	30	..	....	13,600	85	Bronchial.
18	44	..	....	13,600	87	Bronchial.
19	60	..	....	13,300	85	Bronchial.
20	70	M.	5,500,000	13,000	..	Chronic with emphysema.
21	25	..	... .	12,400	90	Bronchial. Diff. count 500 cells: Polynuclear, 64 per cent; lymphocytes, 27; eosinophiles, 9.
22	24	..	....	12,000	75	Eosinophiles, 4 per cent.
23	35	..	....	10,860	65	Bronchial. Diff. count 500 cells: Polynuclear, 75.6 per cent; lymphocytes, 16.6; eosinophiles, 7.8.
24	68	..	....	10,000	85	
25	29	M.	....	9,750		
26	58	..	....	9,400	85	
27	35	..	....	8,000	90	Bronchitis; emphysema Diff. count 400 cells: Polynuclear, 60 per cent; lymphocytes, 30; cosinophiles, 10.
28	29	..	....	8,000	80	Emphysema.
29	62	..	....	7,400	80	Chronic interstitial nephritis.
30	25	..	....	6,600	85	Arteriosclerosis.

For Pneumonia, see page 189.
For Phthisis, see page 291.
For Abscess of Lung, see page 380.

SYPHILIS OF THE LUNG.

In a case of syphilitic infiltration of the lung (autopsy—Drs. Councilman and Wright) recently observed at the Massachusetts General Hospital the leucocytes rose rapidly from 8,700 to 27,400 as death approached.

TABLE LXX.—GANGRENE OF LUNG AND ABSCESS.

Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
49	....	39,900	....	Abscess; autopsy.
42	....	22,400	....	Abscess after grippe.
19	....	18,400	....	Gangrene.
48	4,712,000	16,600	65	November 7th; abscess.
		7,400	....	November 9th.
		20,000	....	November 14th.
		11,900	....	November 16th.
48	....	16,400	....	Abscess after immersion.
54	....	15,300	....	First day; gangrene.
		20,500	....	Fourteenth day.
		18,300	....	Sixteenth day.
		23,000	....	Nineteenth day.
		27,000	....	Twenty-first day.
		27,000	....	Twenty-sixth day.
		31,000	....	Twenty-ninth day.
		17,000	....	Thirty-second day; better.
		20,000	....	Thirty-sixth day.
		15,800	....	Fifty-fourth day.
50	....	9,600	....	Gangrene.
29	....	8,400	80	Abscess.

PART V.

DISEASES OF THE NERVOUS SYSTEM, CONSTITUTIONAL DISEASES, AND HEMORRHAGIC DISEASES.

CHAPTER VIII.

DISEASES OF THE NERVOUS SYSTEM.

NEURITIS.

IN cases of multiple neuritis, febrile and apparently of an infectious nature, the following counts are found in the records of the Massachusetts General Hospital:

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	..	..	4,816,000	25,000	42	July 10th. Temperature 101°.
				24,800	..	July 13th.
				18,700	..	July 16th.
				21,000	..	July 20th.
			4,320,000	16,000	60	July 25th.
				28,700	..	July 31st. No fever.
				19,500	..	August 7th. No fever.
				23,200	..	August 20th. No fever.
2	24	..	....	22,800	70	
3	41	..	....	10,900	85	Brachial.
4	37	..	....	10,400	85	
5	42	..	....	10,300	68	Traumatic.
6	32	..	....	10,100	85	
7	49	..	....	9,600	61	
8	24	..	....	8,400	..	Polynuclear, 36 per cent; lymphocytes, 62; eosinophiles, 2. (Count, 300 cells.)
9	22	..	....	6,400		

The first case, a boy of eleven, recovered and left the hospital well.

But these changes occur also in alcoholic (afebrile) neuritis, as the following counts show:

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	27	..	....	20,800	90	January 31st.
				21,300	..	February 3d.
				11,400	..	February 4th.
2	40	..	....	16,100	..	Pneumonia. No autopsy.
			3,608,000	15,000	75	
			3,260,000	14,000	64	
				13,700	60	
3	39	..	3,584,000	12,000	45	
				11,200	68	
				7,700	80	
4	25	..	....	7,600		
				6,700	82	

In all cases the counts were made just at meal-time, so that the leucocytosis is not due to digestion. Gastritis was not present in either case.

One case of post-diphtheritic neuritis in a child of eight showed the presence of anæmia only: Red cells, 3,850,000; white cells, 7,393; hæmoglobin, 70 per cent.

Neuritis in lead poisoning does not affect the count of leucocytes, as twenty-five cases studied at the Massachusetts General Hospital have shown.

TABLE LXXI.—HERPES ZOSTER.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	52	....	15,500	....	Temperature 99°.
2	46	....	14,000	90	October 23d.
			14,200	....	October 25th.
			15,000	....	October 28th.
3	34	....	10,000	90	
4	74	....	9,100		
5	53	....	8,500	60	
6	65	....	5,700	90	

Neuralgia, whether facial, intercostal, sciatic, or ovarian, showed normal blood in numerous cases examined at the Massachusetts General Hospital.

DISEASES OF THE BRAIN.

Meningitis (see Inflammation of Serous Membranes, page 284).

Zappert in one case of *brain abscess* found only 4,000 white cells.

In *pachymeningitis hæmorrhagica* and *cerebral syphilis* (one case of each) v. Jaksch found leucocytosis. My own experience has been the same.

EPILEPSY.

Pieraccini (*loc. cit.*) records the following:

No.	Age.	Per cent polynuclear.	Per cent lymphocytes.	Per cent eosinophiles.	Remarks.
1	17	74.3	18.1	7.4	During post-convulsive sleep. Patient is an idiot.
2	24	90.3	8.3	1.2	Two hours after convulsion.

TABLE LXXII.—PUERPERAL ECLAMPSIA (PIERACCINI).

No.	Per cent polynuclear.	Per cent lymphocytes.	Per cent eosinophiles.	Remarks.
1	73.7	....	0.2	Uræmic.
	78.2	....	5.3	O. K.
2	87.1	....	0	Eclamptic.
	82.9	....	1.2	O. K.
	77.3	....	2.5	O. K.
3	84.6	....	0	Eclamptic.
	79.6	....	2.6	O. K.
	84.0	....	7.2	O. K.
4	80.3	....	1.2	Eclamptic.
	77.4	....	2.5	O. K.

Cerebral and Cerebellar Tumors.—Von Jaksch found slight leucocytosis in two cases of brain tumor and one of *cysticercosis*. Zappert found normal blood in one case of cerebral tumor.

TABLE LXXIII.—CEREBRAL TUMOR.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	43	..	....	18,100	70	
2	38	..	....	16,900	75	
3	10	..	....	16,200	90	
4	59	..	....	16,200	80	April 7th.
				15,900	..	April 9th.

TABLE LXXIII.—CEREBRAL TUMOR (*Continued*).

	ge.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
				17,000	..	April 11th.
				17,900	..	April 14th.
	5	..	....	16,000	100	
	1	..	....	15,000	80	April 10th. Glioma of the corpora quadrigemina and cerebellum. Autopsy.
				21,600	..	April 20th.
				12,600	..	April 21st.
				24,500	80	June 30th.
				29,900	..	July 18th.
				14,400	..	July 23d.
				19,600	..	July 27th.
				13,100	..	July 29th.
				19,000	..	August 2d.
				31,000	..	August 5th.
				25,200	..	August 10th.
				26,400	..	August 12th.
				21,000	..	August 16th.
				31,400	..	August 19th.
				25,500	..	August 21st.
				26,600	..	August 23d.
				30,800	..	August 25th.
				21,000	..	August 29th.
				29,200	..	September 2d.
				24,000	..	September 6th.
				19,400	..	September 8th.
				17,200	..	September 10th.
				12,000	..	September 12th.
				18,300	..	September 18th. Died October 12th.
7	22	..	....	15,000		
8	13	..	....	14,500		
				18,700		
9	?	..	....	14,400	85	Died.
10	43	..	....	14,000	100	
11	?	..	....	13,100	85	
12	26	..	....	12,500		
13	4	..	....	12,200	70	
14	27	..	....	10,600	60	
15	42	..	....	10,400	80	
16	32	..	....	9,840	70	
17	28	..	....	9,600	68	
18	25	..	....	9,000	90	
19	33	..	....	9,000	72	
20	43	..	....	8,200	90	
21	24	..	....	7,800	90	
22	52	..	....	7,000		
23	60	.	....	5,800	95	
24	31	..	....	4,100		

Fresh cerebral hemorrhage usually causes leucocytosis, as the following table shows:

TABLE LXXIV.—CEREBRAL HEMORRHAGE.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	42	M.	....	81,000	95	Autopsy.
2	52	M.	....	80,000	..	Polynuclear cells, 92 per cent.
			5,512,000	25,000	85	Autopsy.
8	62	..	....	80,000	100	Autopsy.
4	60	..	....	29,700	..	Autopsy.
5	57	..	....	27,000	100	Autopsy, ventricular.
6	19	..	....	24,000	80	Cerebro-spinal, disseminated. Death.
7	60	..	....	28,600		
				26,000	..	Second day.
8	55	..	....	22,200	..	Coma.
9	69	..	....	19,800		
10	65	..	....	19,800	78	Autopsy.
11	47	M.	....	19,400	..	Autopsy.
12	54	..	....	19,000	65	
13	75	..	....	18,800	88	November 17th.
				22,600	..	November 19th.
				16,800	..	November 21st. Autopsy.
14	?	..	....	18,400	80	Multiple with meningeal hemorrhage. Autopsy.
15	47	..	....	18,400	85	Chronic diffuse nephritis.
16	43	..	....	18,000	85	Hemiplegia.
17	63	..	....	17,400	95	Death.
18	56	..	....	17,400	100	Coma. Hemiplegia.
19	49	.	....	17,200	95	
20	70	F.	....	16,800	68	Hemorrhage four days before count. Autopsy.
			5,560,000	15,600	90	
21	70	..	....	16,700	85	Death.
22	50	..	....	16,800	94	March 20th. Right hemiplegia in aphasia.
23	59	..	....	16 000		
24	58	..	....	18,800	..	March 21st.
				15,700	80	Death.
25	2	..	....	15,000	90	Death.
26	62	..	....	14,900	..	Temp, 104.7°. Died.
27	50	..	....	14,500	78	Aphasia.
28	58	..	....	14,000	90	
29	48	..	....	13,800	90	Aphasia.
30	52	.	....	13,800	..	Hemiplegia. Died.
31	53	..	....	13,000	100	Death.
32	48	..	....	13,000	..	Hemiplegia. Coma.
33	51	..	....	12,600	95	
34	?	..	....	12,400	95	Death.
35	37	M.	....	12,300	70	
36	68	..	....	12,000		
				11,900	..	No coma.
37	55	..	....	11,800		
38	42	..	....	11,600		
39	56	..	....	11,200	100	Death.
40	48	..	....	10,800	70	
41	49	.	....	10,500	90	Nephritis. Death.
42	38	M.	....	10,400	58	Conscious; recovered.

E LXXIV.—CEREBRAL HEMORRHAGE (*Continued*).

Sex.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
I.	....	10,300	90	Autopsy.
I.	....	10,200	60	
..	....	10,200	70	
..	....	9,700	80	
..	....	9,200	95	Chronic interstitial nephritis. Death.
.	....	8,200	85	
.	....	8,100	90	
..	....	7,400	85	Hemiplegia.
..	952,000	5,200	18	Arteriosclerosis; emphysema of lungs; pernicious anæmia; temp. 102°. Polynuclear, 84.2 per cent; lymphocytes, 13.8; eosinophiles, 0.8; myelocytes, 0.8; basophiles, 0.2; megaloblasts, 6.

CAISSON DISEASE.

		x.	Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
1	20	..	....	52,000	100	December 19th.
			6,608,000	11,600	..	December 20th.
2	29	..	....	20,200	85	April 15th.
				8,900	..	April 16th. Diff. count 500 cells: Polynuclear, 66 per cent; lymphocytes, 33; eosinophiles, 0.5; mast cells, 0.5.
3	..	..	....	18,900		
4	30	..	....	10,700		
5	42	..	....	7,700	80	August 4th.
				19,200	..	August 5th.
				11,600	..	August 7th.

In a carefully studied case of *intermittent claudication* the following counts were recorded at the Massachusetts General Hospital:

TABLE LXXV.—INTERMITTENT CLAUDICATION.

Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
38	....	21,600	75	January 18th.
		25,200	..	January 20th.
		16,900	..	January 24th.
		10,200	..	January 26th.
		37,400	..	January 30th.

TABLE LXXV.—INTERMITTENT CLAUDICATION (*Continued*).

Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
		25,400	..	February 4th.
		26,200	..	February 11th.
		39,100	..	February 18th.
		45,700	..	February 21st.
		26,200	..	February 26th.
		27,400	..	March 5th.
		31,600	..	March 16th.

CHOREA AND TETANY.

Chorea showed in twelve cases normal blood except for increased percentages of eosinophiles, as in Zappert's four cases, counted 630–1,360 (8–19 per cent) of eosinophiles. Brown[1] confirms this on the basis of twelve observations in a case of chorea. Eosinophiles were constantly increased, five to nine per cent.

Burr[2] has made a careful study of the blood in thirty-six cases and arrived at the following conclusions: There are usually a slight diminution in red cells and a moderate diminution in hæmoglobin. Any severe grade of anæmia is due to some complication. He did not record the leucocytes. Tetany shows no blood changes.

DISEASES OF THE SPINAL CORD.

Chronic diseases of the spinal cord, such as tabes dorsalis, syringomyelia, spastic paraplegia, diffuse myelitis, paralysis agitans, and progressive muscular atrophy, are found to produce no changes in the blood, but acute myelitis may produce marked and persistent leucocytosis, as the following case shows:

TABLE LXXVI.—MYELITIS.

Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
30	....	19,100	90	February 25th. Acute general.
		16,000	..	March 1st.
		15,000	..	March 3d.
		16,000	..	March 5th.
		19,000	..	March 7th.

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[1] Brown: Maryland Med. Journal, July, 1902.

[2] Burr: Univ. Med. Mag., vol. ix., p. 163.

TABLE LXXVI.—MYELITIS (*Continued*).

Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	27,000	..	March 9th.
	27,900	..	March 11th.
	33,500	..	March 13th.
	21,600	..	March 15th.
	21,200	..	March 17th.
	24,200	..	March 19th.
	22,500	..	March 21st.
	19,600	..	March 23d.
	14,500	..	March 25th.
	10,900	..	March 27th.
			March 28th. Diff. count, 500 cells: Polynuclear, 71.2 per cent; small lymphocytes, 23.6; large lymphocytes, 4.4; eosinophiles, 0.8; normoblasts, 1.
	13,700	70	March 29th.
	13,000	..	March 31st.
	16,000	..	April 2d.
	17,600	..	April 4th.
	13,300	..	April 6th.
	26,000	..	April 8th.
	17,000	..	April 10th.
	22,400	..	April 12th.
	17,700	..	April 14th.
	14,600	..	April 16th. Autopsy.

For Spinal Meningitis, see page 284.

GENERAL PARALYSIS OF THE INSANE.

Capps[1] has made a careful study of the blood in nineteen cases and comes to the following conclusions:

1. Red corpuscles and hæmoglobin are always slightly diminished, the averages being 4,789,900 and 85 per cent.

2. Most cases show a slight leucocytosis—22 per cent above the normal on the average. Early cases may have no leucocytosis.

3. The polymorphonuclear leucocytes average nearly 74 per cent and the smaller forms of lymphocytes only 14.2 per cent, while the larger forms of lymphocytes are relatively numerous, averaging 7.8 per cent. In a few cases the eosinophiles were very numerous[2] (8.7 and 6.4 per cent).

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[1] American Journal of the Medical Sciences, July, 1896.

[2] Roncoroni (Archiv. di Psichiat. Scien., 1894, p. 293) finds eosinophiles increased even to twenty-five per cent in the agitated and violent cases.

4. At the time of *convulsions* the red cells and hæmoglobin are apparently increased, due no doubt to the violent muscular contractions which raise blood pressure and concentrate the blood, or to cyanosis.

There is a sudden and pronounced increase in the leucocytes during and after convulsions or apoplectiform attacks. That this is not due to concentration of the blood or to stasis Capps thinks is shown by the fact that not only the number, but the differential count of white cells shows changes, the "*large mononuclear*" *cells being relatively increased*, sometimes as high as 25 per cent. *Myelocytes* were seen in one case after the convulsions, and especially just before death, when in a leucocytosis of 18,250 11 per cent were myelocytes.[1]

HYSTERIA AND NEURASTHENIA: HYPOCHONDRIASIS.

A large number of cases have been counted at the Massachusetts General Hospital with a view of excluding other diseases. The blood count is always normal except that in a certain number of the hysterical cases eosinophiles are relatively increased, and that many of the neurasthenics show the increased percentage of lymphocytes which I have alluded to above (page 106) as characteristic of a variety of debilitated conditions.

Marked anæmia is seldom present, although the hæmoglobin is not infrequently as low as 65 per cent. Reinert[2] found the hæmoglobin under 60 per cent in only 4 out of 48 cases of hysteria, and in *none* of 36 neurasthenics.

The value of the blood examination in such cases, like that of the urine or the lungs in hysteria, is as negative evidence, and in this respect it is important. When the discrepancy between complaints and signs is great, we want to be doubly sure that nothing hidden escapes our notice, and the blood examination is one of the most valuable adjuvants we have in the discovery of deep-seated inflammation or malignant disease, as well as in giving us a general measure of the patient's degree of bodily health as distinguished from nervous force. The former may be high when the latter is low, or both may be low, and the distinction marks out two classes of cases in which somewhat different treatment is appropriate. There is no use in undertaking to make "blood and fat" when the patient has already plenty of each, though it may be well to carry out the same *régime* as a matter of suggestion.

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[1] Leucocytosis has been repeatedly noticed in convulsions from various causes. Probably the irritant which causes the motor discharge also acts on the leucocytes by chemotaxis. For example, Barrows' study of eight cases of insanity with convulsions include counts of: one, 43,000 leucocytes with 92 per cent of polynuclears; two, 33,000 leucocytes with 83 per cent of polynuclears; three, 32,400 leucocytes with 85 per cent of polynuclears and 9 per cent of myelocytes; four, 21,500 leucocytes with 88 per cent of polynuclears. These counts were made immediately after a series of convulsions. The leucocytosis lasted for many hours and showed characteristics of ordinary infectious leucocytosis.

In convulsions from improper feeding in infancy I have seen the leucocytes rise from 13,500 before the fit to 27,800 after it.

[2] Münch. med. Woch., 1895, No. 14.

MENTAL DISEASES.

The association of anæmia with insanity is too frequent to be a mere coincidence, though it is hard to make either serve as a cause for the other. Very possibly they should both be looked upon as symptoms of a common underlying (unknown) cause.

This form of anæmia has been noticed by Houston[1] in melancholia and general paralysis, and by Smith[2] in various forms of insanity.

Krypiakiewicz[3] noticed an increase of eosinophiles in acute forms of insanity, but not in the chronic forms. The *leucocytosis of acute delirium*[4] is exemplified by the following case from the Massachusetts General Hospital records:

A girl of fifteen; acute delirium; leucocytes, 12,750; no food for eight hours; red cells, 4,510,000; hæmoglobin, 63 per cent.

Puerperal mania is to be distinguished from the delirium of puerperal sepsis by the fact that the latter shows leucocytosis with increased percentage of polymorphonuclear cells, while the former has no leucocytosis (if uncomplicated) and the eosinophiles are apt to be increased[5] (diminished in sepsis).

A case of puerperal mania seen by the writer showed: Red cells, 5,210,000; white cells, 6,500; hæmoglobin, 84 per cent; eosinophiles, 8 per cent.

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[1] Houston: Boston Med. and Surg. Journal, January 11th, 1894.

[2] Smith: Jour. of Ment. Science, October, 1890.

[3] Krypiakiewicz: Wien. med. Woch., 1892, No. 25.

[4] Ref. in Klein-Volkmann's "Sammlung klin. Vorträge," December, 1893.

[5] Neusser: *Loc. cit.*

As a result of 92 full and careful blood examinations in 5 cases of depressive-maniacal insanity, Jessie Weston Fisher[1] comes to the following conclusions:

"1. There are no pathognomonic blood changes in cases of maniacal phases of manic-depressive insanity.

"2. Anæmia is not a causative factor nor always an accompaniment of this psychosis.

"3. The hæmoglobin and red cells are frequently, if not always, increased during an attack of excitement.

"4. A leucocytosis is an almost constant accompaniment and, I believe, a result of psychomotor activity."

At the end of three out of five cases the eosinophiles were increased. Earlier in the disease they had been low or normal.

CONSTITUTIONAL DISEASES.

OBESITY.

Oertel distinguishes a plethoric and an anæmic form of obesity not merely clinically, but by the evidence of post-mortem examinations. He believes that there is a real overfilling of the vessels in the first. The second form occurs most often in women.

Kisch examined (with v. Fleischl's instrument) the hæmoglobin of 100 obese patients; 79 showed over 100 per cent of hæmoglobin, 1 reaching 120 per cent, while the other 21 were anæmic.

DIABETES.

There is nothing characteristic about the blood except the increased amount of sugar to be detected (0.57 per cent as against 0.1 per cent normally); but this is not a clinically applicable test.

Two simple tests for diabetic blood have recently attracted attention:

1. Bremer's test: Heat thick-spread blood films to 135° C.; cool and stain with one-per-cent aqueous solution of Congo red for two minutes. The blood if diabetic looks *yellow* to the naked eye. Normal blood similarly treated looks *red*. Staining with methyl blue also shows a difference between normal blood and diabetic blood. The normal is blue, the diabetic yellowish-green.

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[1] Fisher: American Jour. of Insanity, 1903, vol. 59, No. 4.

2. Williamson's test: Make a mixture of:

Blood.	20 c.mm. (2 drops).
Aqueous methyl blue (1:6,000)..............	1 c.c.
Liquor potassæ, 60 per cent (sp. gr., 1.058)	40 c.c.
Water	40 c.c.

Let the mixture stand three to four minutes in boiling water. With diabetic blood the mixture turns yellow, with normal blood it does not. Williamson has found this test positive in eleven diabetics and negative in one hundred cases of other diseases. Bremer claims that by his method cases of diabetes can be recognized before sugar appears in the urine or after it has (temporarily) disappeared. Le Goff confirms the value of the test. Eichner and Folkel find Bremer's reaction to be as stated, but find similar color changes in leukæmia, Hodgkin's disease, and Graves' disease, and changes something like it in a variety of cachectic conditions. Badger has studied the blood of diabetics, leukæmics, cases of Graves' disease, and other cases at the Massachusetts General Hospital. Only in Graves' disease did he find reactions like those of diabetic blood.

TABLE LXXVII.—DIABETES WITH COMPLICATIONS.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	8	....	49,000	..	Coma.
2	58	....	26,000	65	Coma.
3	65	....	20,000	75	April 11th. Gangreme of toes.
			14,600	..	April 14th.
			16,600	..	April 18th.
			16,300	75	April 22d.
			17,100	..	April 26th.
4	22	....	17,000	84	Coma.
5	53	....	12,500	80	Coma.
6	60	....	8,200	80	Gangrene.
7	..	....	4,200	..	Coma.

The alkalinity has been said to be greatly diminished, especially in the fatal coma, but v. Noorden thinks the tests are unreliable.

Fat is often increased in the blood up to about twelve times the normal, so that the serum is milky, and glycogen has been demonstrated microchemically in the corpuscles.

Red Cells.

Sugar in the blood draws water from the tissue into the vessels, thereby *diluting the blood ;* but in a short time the blood frees itself of the excess of sugar and fluid through increased diuresis so as to *concentrate the blood.*

These two alternating influences serve to explain the widely different counts of different observers.

Toward the end of the disease a decided *cachexia* often develops, the anæmia of which may be temporarily covered up by the concentration above noted, or accentuated by the *dilution* which sometimes occurs. Accordingly we may find the corpuscles increased, normal, or diminished in different cases or at different times with the same case.

Grawitz counted 4,900,000 red cells in a patient in comparatively good health, and three weeks later, when the patient had just been seized with the fatal coma, the count showed 6,400,000 per cubic millimetre. With the iodine gum-arabic mixture extracellular brown stained-masses are often very much more abundant than in normal blood.

The white cells show no constant changes, except that v. Limbeck has noted in several cases that the digestion leucocytosis is unusually large even without previous fasting. Von Jaksch found leucocytosis in one of his eight cases, but on this point as on many others his results are almost unique. The only similar observation is that of Habershon,[1] who reports moderate leucocytosis, decreased by strict diet. In thirteen cases I have never seen leucocytosis except in the presence of complications (see table, page 392).

GOUT.

A few cubic centimetres of serum from gouty blood made acid with acetic acid (six drops of a twenty-eight-per-cent solution to every drachm of serum) deposit crystals of uric acid on a thread in from eighteen to forty-eight hours; but this is not always to be found, and is by no means peculiar to gout.[2] Uric acid is to be found in the blood in pneumonia, cirrhotic liver, nephritis, grave anæmia, leukæmia, and gravel; also in health and after a meal of calf's thymus or any food containing much nuclein.

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[1] St. Bartholomew's Hosp. Report, 1890, p. 153.

[2] It is important to evaporate the serum at a temperature not above 70° F., otherwise crystals will not form.

The red corpuscles show no special changes except in severe chronic cases, which are sometimes anæmic. The white cells are increased according to Neusser, while v. Limbeck and Grawitz found the blood wholly normal.

It is particularly in this disease that Neusser supposed the "perinuclear basophilic granulations" to exist in the white cells, which condition he believes to be characteristic of any "uric-acid diathesis." Futcher has conclusively disproved this. Fibrin is increased in acute cases.

Ewing states that he found "uniform but moderate anæmia in a series of chronic cases examined at Roosevelt Hospital, the patients all coming from the poorer classes. In the chronic cases leucocytosis of moderate grade may be observed, but it is difficult to determine its relation to the gouty process, as many of these patients suffer from other complaints." I have records of only two cases, one a chronic case with huge tophi showed in an acute exacerbation 21,000 leucocytes with 70 per cent hæmoglobin. A severe subacute case showed 15,000 leucocytes. Da Costa records 14,000 in a single case with polycythæmia (7,125,000).

Watson[1] records the following:

Date.	Leucocytes.	Remarks.
June 7th	9,000	No symptoms.
June 12th	12,500	Slight symptoms.
June 20th	20,500	At height of attack.

MYXŒDEMA.

Le Breton[2] examined the blood in one case both before and after thyroid treatment, and found that after forty days' treatment the red cells had risen from 1,750,000 to 2,450,000, the white cells from 4,500 to 9,600, and the hæmoglobin from 65 to 68 per cent.

The remarkably high color index in this case before treatment (nearly 2!) corresponds with the observations of Le Breton in the dried specimen, which showed a decided increase in the size of the red corpuscles. He also noticed, before instituting the thyroid treatment, the presence of nucleated red cells and an excess of the polymorphonuclear form of leucocytes. Under treatment the nucleated red cells disappeared and the lymphocytes rose to their normal per cent.

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[1] Watson: Brit. Med. Jour., 1900, p. 10.

[2] Le Breton: Ref. in Wien. med. Blätter, 1895, p. 49.

Putnam[1] has watched a similar case in which the number of red cells rose from 3,120,000 to 5,700,000 under thyroid treatment.

Murray[2] has collected 23 cases with blood examinations. Of these cases, 7 showed a normal blood count, 10 were anæmic, 4 showed leucocytosis, and 2 exhibited both anæmia and leucocytosis.

Kraepelin[3] noticed (like Le Breton) a marked increase in the average diameter of the corpuscles in three cases, even when the count and the hæmoglobin were normal. Traina (*Centralbl. f. allg. Path.*, etc., April 15th, 1901) in *cachexia strumipriva* found a leucocytosis of 18,000 to 32,000 with 75 to 80 per cent of polynuclear cells, lasting for one or two weeks after the operation, and Mezinescu (ref. in *Arch. gén. de Méd.*, 1902, p. 743) in a similar case counted 49,000 leucocytes with 84 per cent of polynuclear cells.

I have had an opportunity to examine the blood in ten cases of this disease, but did not find anything remarkable in any one of them.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	58	4,700,000	11,400	65	March 21st.
			8,600	60	April 1st.
		4,328,000	9,800	80	April 6th.
2	47	....	10,800	65	
3	..	4,460,000	8,800		
4	41	4,098,000	7,900	58	
5	..	4,062,000	7,900		
6	46	....	6,000	80	
7	..	4,670,000	6,000	87	
8	..	4,856,000	5,200	80	

Differential counts were made in five cases, and no increase in the size of the corpuscles, such as Le Breton and Kraepelin saw, was present in these cases. The count showed:

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[1] Putnam: Ref. in Murray's article in "Twentieth Century Practice of Medicine," vol. iv.

[2] Murray: "Twentieth Century Practice of Medicine," vol. iv., p. 710.

[3] Kraepelin: Deut. Arch. f. klin. Med., vol. xlix., p. 587.

Case.	Polymorphonuclear cells.	Lymphocytes.	Eosinophiles.
1	67.0	28.0	5.0
2	67.0	27.8	4.4
3	74.0	26.0	
4	66.0	31.5	2.5
5	77.8	21.6	.6

The increase of eosinophiles in two of these cases may perhaps be due to the skin troubles in the disease.

J. J. Thomas found a few myelocytes in a case of Putnam's.

CRETINISM.

Koplik[1] records the following in two cases of sporadic cretinism:

Case I.—Fifteen months old; advanced stage of disease. Hæmoglobin, 18 per cent.

Case II.—Red cells, 3,026,000; white cells, 13,500; hæmoglobin, 105 per cent. This high hæmoglobin corresponds to *normal fœtal* blood. The child was nine weeks old, but its backward development is mirrored in the blood. As the case improved under thyroids the hæmoglobin came down.

GRAVES' DISEASE (BASEDOW'S DISEASE; EXOPHTHALMIC GOITRE).

The blood is normal, except for an occasional associated chlorosis and sometimes a marked lymphocytosis. In one case I found 51.3 per cent of lymphocytes and 1 per cent of myelocytes in 1,000 leucocytes, the polymorphonuclear cells being only 48 per cent; but in fourteen other cases I have never found this again. The same fact has been noticed by Neusser (cited in Klein, *loc. cit.*).

Oppenheimer[2] found the red cells and hæmoglobin normal in two cases. Von Jaksch[3] in one case "complicated with myxœdema" found 3,818,000 red and 8,000 white cells.

The association of Graves' disease with chlorosis is illustrated by two cases from Zappert:[4]

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[1] New York Medical Record, October 2d, 1897.

[2] Deut. med. Woch., 1889, p. 861.

[3] Zeit. f. klin. Med., 1893, p. 187.

[4] Zeit. f. klin. Med., 1893, p. 266.

Case.	Red cells.	White cells.	Per cent Hæmoglobin.
1....................	2,858,000	8,800	82
2....................	2,738,000	8,800	80

The same writer found eosinophiles increased (8.5 per cent) in one out of four cases

Table LXXVIII.—Massachusetts General Hospital Cases.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	44	M.	3,668,000	2,800	45	
2	36	..	....	5,600	80	March 29th.
				6,800	..	May 20th.
3	42	..	....	7,000	75	
4	39	..	....	7,100	70	
5	27	..	....	7,300	65	
6	42	.	4,920,000	7,700	60	
7	34	..	....	8,500	85	
8	31	..	....	8,700	80	
9	51	..	....	9,800	90	
10	33	..	4,464,000	9,800	63	Died.
11	19	..	....	10,200	80	
12	46	..	....	10,500	80	
13	28	..	....	11,500	70	
14	41	..	....	11,600	90	
15	44	..	....	12,500	50	January 13th.
			4,584,000	12,700	..	January 31st.
				16,000	56	February 13th.
				15,000	..	February 15th.
16	35	..	....	14,400	70	March 1st.
				7,600	..	March 8th.
				6,800	..	March 15th.
17	29	..	3,483,000	17,800	50	
18	40	..	....	23,100	70	February 10th.
				21,400	..	February 11th.

Table LXXIX.—Goitre Without Exophthalmos.

No.	Age	Red cells.	White cells.	Per cent hæmoglobin	Remarks.
1	46	....	12,000	75	
2	21	....	11,000	80	
3	17	5,448,000	7,400	55	
4	51	....	6,600	90	
5	45	....	5,800	65	

ADDISON'S DISEASE.

Some, but not all, cases are accompanied by marked anæmia. Neumann[1] observed a case in which the symptoms came on acutely and the red cells sank to 1,120,000 per cubic millimetre. During the convalescence which followed, the cells ran up above normal, reaching 7,700,000.

Tschirkoff[2] reports two cases in which the red cells were respectively 3,280,000 and 2,933,000 at the lowest, but whose hæmoglobin was extraordinarily high, over 100 per cent in one case. This he found on spectroscopic examination to be due to a great increase of reduced hæmoglobin in the corpuscles. Methæmoglobin was also noted.

The white corpuscles showed no changes, quantitative or qualitative, except that they contained black pigment granules. Three cases have been examined at the Massachusetts General Hospital. The first, a woman of thirty, showed 6,240,000 red cells with 14,000 white, and 90 per cent of hæmoglobin. The differential count of 90 leucocytes showed the following figures: Polymorphonuclear cells, 53.4 per cent; lymphocytes, 41 per cent; eosinophiles, 4.5 per cent; myelocytes, 0.9 per cent.

The eosinophiles were very large, some of them eosinophilic myelocytes.

The second, a man of forty-two, was very anæmic and weak at entrance and showed: Red cells, 2,196,000; white cells, 7,500; hæmoglobin, 20 per cent. Differential count of 200 leucocytes showed: Polymorphonuclear cells, 65 per cent; lymphocytes, 31.5 per cent; eosinophiles, 3.5 per cent; 5 normoblasts; marked poikilocytosis.

Under suprarenal extract his blood improved in a month till his red cells numbered 4,700,000; white cells, 9,000; hæmoglobin, 65 per cent.

The third, a man of fifty-two, showed: October 20th—red cells, 2,848,000; white cells, 4,800; hæmoglobin, 45 per cent. December 10th—red cells, 2,624,000; white cells, 7,100; hæmoglobin, 45 per cent. Differential count: Polynuclear, 74 per cent; small lymphocytes, 22 per cent; large lymphocytes, 4 per cent; eosinophiles, 0.4 per cent. No nucleated red cells.

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[1] Neumann: Deut. med. Woch., 1894, p. 105.

[2] Zeit f. klin. Med., 1891, vol. xix., Suppl.-Heft 87.

A fourth patient, kindly sent me by Dr. Rogers, of Dorchester, showed: Red cells, 2,864,000; white cells, 2,000; hæmoglobin, 51 per cent. Differential count of 300 cells showed: Polymorphonuclear cells, 63.3 per cent; lymphocytes, 33.3 per cent; eosinophiles, 2.3 per cent; basophiles, 0.3 per cent.

Brown[1] mentions 2 cases with 4.4 per cent and 8 per cent of eosinophiles (286 and 960 absolutely).

I have never seen melanin in the leucocytes as Tschirokff did in his two cases.

TABLE LXXX.—ADDISON'S DISEASE (ADDITIONAL CASES).

Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
34	5,056,000	5,000	60	Soon died.
39	5,460,000	7,000	80	Autopsy.
29	4,804.000	10,000	68	Polynuclear, 77.6 %. Lymphocytes, 14.0 Eosinophiles, 8.0 Myelocytes, .4
	519,200	10,400	80	

DISEASES OF BONE.

TABLE LXXXI.—OSTEO-ARTHRITIS.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	58	3,552,000	49,000	50	November 11th. Spine.
			32,000	..	November 12th.
			35,000	..	November 14th.
			28,800	..	November 17th.
			24,000	..	November 20th.
			22,500	..	November 23d.
			18,000	..	December 8th.
2	63	....	23,000	80	Spine.
3	53	....	20,400	70	Spine.
4	29	....	14,600	70	Spine.
5	52	....	12,000	85	Spine.
6	52	4,968,000	11,200	70	Spine.
7	21	....	11,000	85	Spine.
8	52	....	10,800	100	Spine.
9	47	....	10,000	85	Spine.
10	58	....	9,800	85	Spine.
11	48	... .	9.000	65	Spine.
12	36	....	9,000	85	Spine.
13	35	....	8,700	80	Spine.

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[1] Internat. Clinic, vol. iv., 12th series.

TABLE LXXXI.—OSTEO-ARTHRITIS (*Continued*).

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
14	37	....	6,600	90	Spine. Diff. count: Polynuclear, 62 per cent; small lymphocytes, 30; large lymphocytes, 7; eosinophiles, 1.
15	42	....	5,200	75	Spine.

TABLE LXXXII.—OSTEITIS DEFORMANS.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	45	....	7,000	80	February 6th.
		4,480,000	10,000	75	February 8th.
2	49	5,330,000	7,200	65	Diff. count: Polynuclear, 66 per cent; small lymphocytes, 33.5; large lymphocytes, 33.5; eosinophiles, 5.
3	37	....	8,600	90	

FRACTURES.

Thirty-five cases of fractures studied by Cabot, Hubbard, and Blake (*loc. cit.*) showed nothing abnormal.

OSTEOMALACIA.

The blood has a long time been supposed, on the authority of v. Jaksch (*Zeit. f. klin. Med.*, vol. xiii., p. 360), to exhibit a diminished alkalinity, the bones being supposed to be eaten away by acids in the blood. Von Limbeck and many other observers have lately shown that the blood is normal in alkalescence.

Corpuscles and hæmoglobin are usually within normal limits quantitatively, but Neusser reports an increase of eosinophiles and the presence of myelocytes in the blood.

Ritchie[1] confirms Neusser and found also that the lymphocytes were more numerous than normal.

Fehling,[2] Sternberg,[2] Chrobak[2] found no increase of eosinophiles.

Rieder's case was normal in all respects: Red cells, 4,892,000; white cells, 5,600; eosinophiles, 3.6 per cent; polymorphonuclear cells, 61 per cent.

[1] Edin. Med. Journal, June, 1896.

[2] Cited by Ritchie: *Loc. cit.*

Ewing says: "The usual condition of the blood in osteomalacia appears to be that of moderate secondary anæmia. The leucocytes have varied from subnormal to moderately increased numbers. The lymphocytes are usually very numerous, an excessive proportion (maximum 56 per cent) having been found by Tschistowitch. High normal proportions of eosins have been found by several observers, but not by others."

RICKETS.

1. Anæmia is always present in severe cases and often in moderate ones. This, together with the fact that many cases of rickets are associated with an enlargement of the spleen, has led to the use of the misleading term "splenic anæmia." There is no form of anæmia found in rickets that may not be found in other conditions (Morse).[1]

Hock and Schlesinger found an average of 2,500,000 red cells in a considerable number of cases with and without enlarged spleen.

Von Jaksch describes a case in which the red cells sank from 1,600,000 to 750,000 within three months, and Luzet saw a similarly rapid process, the cells falling from 2,110,000 to 1,596,000 within three weeks. On the other hand, in Morse's admirable study of twenty well-marked cases the red cells averaged over 4,500,000 and not a case fell below 3,500,000.

2. The hæmoglobin is always relatively low; it averaged 63 per cent in Morse's cases, a color index of about 0.7. Felsenthal got similar results.

White Corpuscles.

It is often difficult to say whether or not the leucocytes are increased, owing to the occurrence of most cases in infants at an age when leucocytes are always higher than in adults—how much higher at any given age depends largely upon the degree of vigor and forwardness of development of the individual child.

In Morse's series, for example, the average age of the infants is twelve months. And for this age none of the counts in his series seems to me necessarily abnormal. They are all under 16,000 except three, these three being 17,900, 18,800, and 22,000 respectively, the latter in a nine months' infant. Many of the counts seem to me subnormal for infancy (5,500, 7,200). Most observers find leucocytosis present in many cases, but not in all.

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[1] Morse. Boston City Hosp. Rep., 1897.

QUALITATIVE CHANGES.

Red Cells.

n all anæmias of infants, the "degenerative" and "regener-" changes are relatively common.

ychromatophilic forms and nucleated corpuscles are fre- ntly to be found, the latter often in great numbers but with a rity of the normoblast type.

White Cells.

Lym tosis is said to be marked, but, as with the question s, we are never quite sure whether the numbers are *for that age*, for lymphocytosis is the normal condition in blood.

, however, as in a case mentioned by Rieder, we find 75 es in every 100 leucocytes, the child being four years old, urely dealing with a pathological condition. Another of s, a seven-months' child, rachitic, with 57 per cent of lym- ytes, seems to fall within normal limits. Not so with Morse's cases. The highest percentage of lymphocytes in his series was 69, in an infant of two months. I have similar counts in health at that age. The average of his twenty cases is 43 per cent, which is, if anything, rather low for that age. The same difficulty arises with regard to the reports of *eosinophilia* in rickets, since eosinophiles are always relatively numerous in infancy. Morse's highest figure was 7 per cent, his average 3 per cent. Hock and Schlesinger found 20 per cent in one subject, and Weiss 16 per cent in another. They were highest in cases with splenic tumor. In Rieder's four cases and in the three seen at the Massachusetts General Hospital, no eosinophilia was present. Myelocytes in small numbers (0.5-0.2 per cent) are not uncommon, and may be considerably more numerous.

CHAPTER IX.

HEMORRHAGIC DISEASES. HÆMOLYSIS AND BLOOD POISONS.

PURPURA HÆMORRHAGICA.

The blood is practically that of anæmia from hemorrhage (red cells and hæmoglobin reduced, white cells increased, occasional nucleated red corpuscles or polychromatophilic forms). Agello[1] has found methæmoglobin in the blood, and hence concludes that the disease is a poisoning of the corpuscles by ptomaïns absorbed from the intestine.

The blood plates are much diminished and may be entirely absent in the worst stages.

Bacteria of various kinds have been reported in the disease, but negative results are also common, and their presence is probably not significant.

The red cells may fall as low as 2,500,000, but are much oftener slightly or not at all diminished. In many mild cases there are *no* demonstrable blood changes. On the other hand, Osler mentions a case which sank to 1,800,000, and in Muir's case the count reached 800,000 with 11 per cent of hæmoglobin. The loss of blood may give rise to a fatal anæmia of the microcyte type (see page 146). In a case of *acute infectious purpura* ("typhus angeiohematique") Barjon and Cade (*Soc. d. Biol.*, 1901, p. 246) found 85,000 leucocytes (94 per cent polynuclears) at the outset, gradually falling to normal within two weeks. The red cells fell to 2,027,000.

Bensaude[2] has observed that in 16 cases characterized by *large hemorrhages* (2 = acute "infectious," 2 with tuberculosis, 2 chronic, 10 = Werlhof's disease) the clot shows no retraction and no transudation of the serum. Cases with *small hemorrhages* (toxic, rheumatic, cachectic, and nervous) do not show any such abnormal characteristics. Hence he concludes that at the outset of a case of purpura, observation of the clotting process may enable us to foretell whether or not the case is to be of a *severe* or of a *mild* type. He found the blood lesion above described to be greatest during the hemorrhagic crises, slowly disappearing between them. Hayem has confirmed these observations. He finds the fibrin network almost invisible. Despite this and despite the absence of contraction in the clot, the actual rate of clotting is normal. Hayem has seen similar failure of contraction when the blood plates are plenty. It occasionally occurs in symptomatic purpura (*e.g.*, from phthisis).

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[1] Riforma Med., Napoli, 1894, p. 103.

[2] La Semaine Méd., 1897, p. 21.

SCURVY.

There are no characteristic blood changes known. When hemorrhage is severe the red cells may sink very low,—to 370,000 as in Talley's[1] case, to 557,875 in a case of Bouchut's;[2] Ouskow[3] and Hayem saw counts of 3,500,000 and 4,700,000. Talley has recently collected from the literature several cases with less than 2,000,000 red cells per cubic millimetre, but the average of the counts of seven observers (see Talley's bibliography) was between 3,000,000 and 4,000,000. The usual qualitative changes of secondary anæmia are present in severe cases; the hæmoglobin suffers as usual more than the count of red cells and is slow in regeneration.

Leucocytes may be increased, whether from hemorrhage or from some complicating inflammatory process, but in uncomplicated cases they are usually reduced (*e. g.*, 4,700 in Talley's case).

"The red cells vary in number and size according to the length and severity of the disease. On account of the frequency of inflammatory complications and hemorrhages the leucocytes are usually increased, Ouskow[3] finding them as high as 47,000, Henry[4] 20,000 in two cases, and Stengel[5] 40,000 (after hemorrhages) with lymphocytosis. Litten, however, observed no leucocytosis, and the writer in two well-marked but uncomplicated cases found no increase" (Ewing). In a single case I recorded: Red cells 3,600,000; white cells, 3,600, hæmoglobin 40 per cent.

[1] Talley: Jour. Am. Med. Assn., November 1st, 1902.
[2] Bouchut: Gaz. des Hôp., 1878, p. 1137.
[3] Ouskow: Centralbl. f. inn. Med. 1878, No. 28.
[4] Henry: Phil. Hosp. Rep., 1890, p. 125.
[5] Stengel: "Twentieth Cent. Pract.," vol. vii.

INFANTILE SCURVY (BARLOW'S DISEASE).

Da Costa in 7 cases found the hæmoglobin ranging from 35 to 65 per cent (average 43 per cent), and the red cells from 2,950,000 to 5,100,000 (average 3,527,000). Only one case showed leucocytosis, the average in 7 being 15,500. The lymphocytes in 4 of the 7 were between 60 and 65 per cent. The eosinophiles were normal or low, and myelocytes 1 to 6 per cent (average 2.5 per cent).

Barlow's disease may lower the red cells as far as 976,000—as in a case of Reinert's—the hæmoglobin being 17 per cent and the white cells 12,000. This was the day before death. The blood plates are not diminished, and the clot retracts normally

HÆMOPHILIA.

The blood changes are practically those just described and show nothing characteristic of the disease. Coagulation is slower than normal and blood plates are sometimes very scanty. The white cells are sometimes persistently diminished, as in the following cases:

I.

	Sept. 11th.	Sept. 14th.	Sept. 17th.	Sept. 20th.	Sept. 23d.	Sept. 24th.
Red cells...........	2,960,000	....	....	....	....	3,800,000
White cells.........	3,400	3,400	3,800	3,900	3,700	3,300
Hæmoglobin	42 per cent.	....	....	....	64 per cent.	49 per cent.

II.

February 8th.	February 28th.	
4,400,000	3,600,000	Daily nose-bleed.
5,000	5,000	
30 per cent.	28 per cent.	

HÆMOLYSIS AND BLOOD POISONS.

The subject is a very extensive one, and I shall not attempt to review the magnificent work of Ehrlich and his pupils except where it concerns the field of practical blood diagnosis. For clinical purposes blood poisons are conveniently divided into three classes:

I. Those that produce hæmolysis alone.

II. Those that produce methæmoglobinæmia and hæmolysis.

III. Those that poison the blood by forming a chemical union with the red cells (other than methæmoglobin) and so interfere with their functions.

I. Hæmolytic Agents.

Among the agencies which produce hæmolysis the most important are:

1. *Infectious diseases*, especially malaria and yellow fever; less often severe sepsis, typhoid, scarlet fever, and Weil's disease.

2. In the course of exhausting diseases such as nephritis, cirrhosis, and those leading to chronic icterus, autohæmolytic substances are not infrequently formed in the system; so also in puerperal eclampsia (Hayem) in the new-born (Winckel's disease), and after the absorption of peritoneal hemorrhage from extra-uterine pregnancy.

3. *Poisons of vegetable origin*—such as those contained in many species of mushrooms, aspidium, felix mas, saponin substances, *i.e.*, the glucocides contained in Quillaja saponaria, the Alpine violet (Cyclamen Europæum), various species of solanum (*night shade*, etc.), various arrow poisons. Probably akin to these are:

4. *Snake poisons* and *scorpion poison* and

5. Guiacol, and quinine under certain conditions.

6. Hæmolysis results from the transfusion of alien blood or of saline solutions not isotonic, from inhaling AsH_3 and rarely from *severe burns*.

7. Under conditions very little understood influences such as cold, fatigue, or emotional strain produce in certain individuals sudden brief hæmolysis to the results of which we give the name of *paroxymal hæmoglobinæmia*.

The process of hæmolysis includes:

1. Separation of the hæmoglobin from the corpuscles so that it colors the serum.

2. Actual breaking to pieces of the red cells without separation of the hæmoglobin.

If normal blood is drawn and left to stand, the serum which separates from the corpuscles is not red-tinged or but very slightly so, *provided* all shaking and jarring are avoided. A very slight reddish tinge may appear in the serum even with most careful technique. In some conditions the hæmoglobin, while not actually separated from the corpuscles within the vessels, is so loosely connected to them that a considerable quantity separates post mortem and colors the serum in spite of the avoidance of any jar.

This condition is to be distinguished from true hæmoglobinæmia, in which the serum is actually colored before leaving the vessels, although the two conditions really represent only different degrees of vulnerability of the red cells.

We are surer of a diagnosis of hæmoglobinæmia when we find bits of broken-down cells in the fresh blood and the additional evidence of hæmoglobinuria or jaundice.

The Blood in Paroxymal Hæmoglobinæmia.

Coagulation is very rapid, but the clot soon dissolves again (Hayem). The fresh blood occasionally shows deformities in the corpuscles or bits of broken cells, and lack of rouleaux if examined during a paroxysm. As a rule the corpuscles of the peripheral blood look normal. Frazer has recently reported a case in which he excited a paroxysm by a cold bath, and studied the blood with great care.

Time.	Red cells.	White cells.	Per cent hæmoglobin.	Blood plates.
10 A.M. Before bath....	4,075,000	15,000	50	450,000
11:05 A.M. Twenty-five minutes after bath; urine pale.	3,633,300	21,800	50	696,000
11:45 (urine dark).......	3,760,000	21,300	60	525,000
1:15 P.M................	4,200,000	21,500	50	**4,250,000** (!)
8:45 P.M................	3,800,000	17,700	50	1,600,000
Next day, 1 P.M.........	4,100,000	18,700	50	500,000

The enormous increase of "blood plates" is striking. It is difficult to resist the conclusion that these blood plates were bits of broken red corpuscles. The serum was current-jelly colored. The appearance of the corpuscles was quite normal.

The Blood in Severe Burns.

I have no personal experience with cases in which hæmolysis has been demonstrated. Locke's[1] careful study of ten cases and of the literature led him to the following conclusions:

1. The blood flows sluggishly and is of a peculiar dark purple appearance.

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[1] Locke: Boston Med. and Surg. Jour., October 30th, 1902.

2. An immediate increase in the number of erythrocytes, in severe but not fatal cases, of from 1,000,000 to 2,000,000 per cubic millimetre takes place within a few hours; in fatal cases there is an increase of from 2,500,000 to 4,000,000 per cubic millimetre.

3. A rapidly increasing leucocytosis occurs in all cases; in those ending in recovery the increase is often 30,000 or 40,000 per cubic millimetre; in fatal cases usually above 50,000 per cubic millimetre.

4. Morphological changes in the erythrocytes are slight.

5. The percentage of neutrophiles is somewhat above the normal, but not so much as in the ordinary inflammatory leucocytosis.

6. A considerable destruction of the leucocytes takes place, especially in the very severe burns.

7. Myelocytes may be present in small numbers in severe cases.

8. There is, as a rule, marked increase in the number of blood plates.

The table on page 409 shows Locke's results in detail.

Ether Inhalation.

Da Costa and Fish (*loc. cit.*) have shown that in anæmic patients ether narcosis may produce a considerable diminution in the red cells and hæmoglobin presumably through hæmolysis (see above, page 253).

II. Poisons Producing Methæmoglobinæmia with and without Hæmolysis.

One of the most important is:

1. *Chlorate of Potash.*—This destroys the corpuscles and produces hæmoglobinæmia and the usual train of symptoms (jaundice, dark urine, etc.) due to this.

Brandenburg[1] examined the blood of a woman who had taken two and one-half ounces of chlorate of potash in water the night before. The blood showed *marked* leucocytosis and broken and distorted red cells. In gross it was chocolate-colored and the serum

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[1] Berliner klin. Woch., 1895, No. 27.

Cases.	Time after accident.	Hæmoglobin, per cent.	Count red blood corpuscles.	Count white corpuscles.	Neutrophiles, per cent.	Lymphocytes.			Eosinophiles, per cent.	Mast cells.	Myelocytes, per cent.
						Small, per cent.	Large, per cent.	Transitional, per cent.			
No. 1	2 hours	....	4,500,000	10,000	77¼	13¾	4	4⅙	0	⅙	0
	19 hours	....	5,460,000	7,000	63⅓	20	7	7⅔	1⅔	⅓	0
No. 2	15 minutes	....	5,822,000	24,000							
	2 hours 30 minutes	....	7,155,000	22,000	59¾	24	7⅙	7⅙	1	¼	0
No. 3	1 hour 15 minutes	....	6,882,000	17,500	63	24⅔	2⅓	7⅓	⅔	2	0
	3 hours 45 minutes	....	6,442,000	28,000	87	7⅓	1⅓	4	1	0	0
	24 hours	95	6,900,000	18,000	82⅔	12	1⅓	3⅓	⅓	⅓	0
	72 hours	98	6,860,000	14,000	79⅔	11	2⅓	6⅔	⅓	0	0
	96 hours	....	5,489,000	13,000	80⅔	10	1⅓	7⅔	½	0	0
No. 4	2 hours	100	7,266,000	16,000	71	22⅔	2⅔	2⅔	1	⅓	0
No. 5	2 hours	....	6,200,000	30,000	86⅓	5⅔	1	7	0	0	0
	19 hours	....	9,250,000	40,000	82	9⅔	3⅓	5	0	0	0
No. 6	30 minutes	....	....	30,000	67	23½	1⅓	5⅔	2⅔	0	0
	15 hours 30 minutes	98	9,244,000	32,000							
	22 hours 30 minutes	....	....	46,200	72⅔	15⅓	6⅓	5⅔	0	0	0
No. 7	2 hours	....	6,820,000	20,000	82	10⅔	2⅔	4⅓	⅓	0	0
	6 hours	....	9,152,000	54,000	84⅔	7⅓	2⅔	5⅓	0	0	0
No. 8	1 hour 15 minutes	....	6,382,000	51,000	73	16	6	2	⅓	⅔	0
No. 9	30 minutes	....	....	78,000	47	41⅓	1⅔	1⅔	2⅔	⅓	5⅓
No. 10	1 hour 15 minutes	....	....	31,000	63	27⅓	7	1⅔	1	0	1
	1 hour 30 minutes	....	....		58⅚	33⅓	1⅓	5⅔	0	1	0
	2 hours	....	....	42,000							
	2 hours 15 minutes	....	8,910,000								

after separation of the clot was brown. The red cells progressively decreased as follows:

	Red cells.	White cells.
First day	4,300,000	20,000
Second day	2,500,000	
Fourth day	2,300,000	
Fifth day	2,100,000	
Sixth day	1,900,000	
Seventh day	1,600,000	15,000 (death).

Jacob[1] studied a similar case: Thirty hours after a dose of 25 gm. of KClO$_3$ the blood showed: Red cells, 4,425,000; white cells, 80,000 (stained specimen resembles leukæmia). Next day, red cells, 1,825,000 (broken and decolorized); white cells, 60,800 Fourth day, red cells, 2,225,000; white cells, 14,000.

2. Ehrlich and Lindenthal[2] report the case of a patient who was poisoned with nitrobenzol. Ten hours after the blood was chocolate-colored and showed methæmoglobin bands. Under the microscope there were no changes till the third day, when poikilocytosis appeared.

	Red cells.	White cells.	Per cent hæmoglobin.	Nucleated red cells per cubic millimetre.
Fifth day	2,275,000	Much increased.	55	2,070
Seventh day	1,845,000	" "	50	7,900
Eleventh day	1,600,000	" "	44	24,700 (!)
Fifteenth day	905,000	" "	40	12,000
Seventeenth day.	1,102,000	" "	..	1,300
Nineteenth day	900,200	" "	..	540
Nineteenth day, death.				

The nucleated red cells were at first mostly normoblasts; later mostly megaloblasts. Posselt[3] and Boas[4] have published similar cases.

3. *Antipyrin and Acetanilid.*—A patient of P. K. Brown,[5] five

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[1] Berl. klin. Woch., 1897, No. 27.

[2] Zeit. f. klin. Med., 1896, p. 427.

[3] Wien. klin. Woch., 1897, No. 30.

[4] Deut. med. Woch., 1897, No. 51.

[5] Brown: Am. Jour. of the Med. Sciences, December, 1901.

days after taking sixty grains of acetanilid showed the following blood:

Hæmoglobin.[1]	Erythrocytes.	Leucocytes.	Nucleated red cells.
5th day of illness, 40 per cent.......	2,200,000	62,400	17,600
6th " " 35 "	1,490,000	62,935	25,705
7th " " 33 "	1,400,000	51,400	19,000
8th " " 32 " (death)	1,166,000	66,450	22,150

TABLE LXXXIII.—DIFFERENTIAL COUNTS.

	NUCLEATED RED CELLS. (Seen during a count of 500 leucocytes.)			LEUCOCYTES.			
	Megaloblasts.	Normoblasts.	Microblasts.	Polymorphonuclear.	Large lymphocytes	Small lymphocytes.	Eosinophiles.
5th day	39	60	1	70 per ct.	26 per ct.	4 per ct.	0
6th day	15	73	12	59 "	30 "	9 "	2
7th day							
8th day (death)	19	65	16	57 "	35.6 "	6.5 "	0

Among the large lymphocytes are included a considerable percentage of myelocytes.

The specimen of the fifth day showed the direct action of the poison on the red cells. The cells were of all sizes and shapes, the microcytes showing an unusual sort of distortion, unlike crenation or the changes in microcytes of pernicious anæmia, and the megalocytes having no distortion and resembling strikingly those of pernicious anæmia. Indeed, as the process advanced the picture of the red cells grew more and more like pernicious anæmia. The average diameter of the cells increased, the microcytes grew fewer in number and showed less distortion, and the color index rose very high.[2]

In Stengel's[3] chronic case of acetanilid poisoning, which eventually recovered, the red cells fell to 2,092,300 with 35 per cent of hæmoglobin and 39,100 leucocytes. Of the red cells 32,000 per cubic millimetre were nucleated, nine-tenths of them being normoblasts. Every known anomaly of staining reaction was present. T. R. Brown[1] mentions an acute case with 12 per cent of eosinophiles (3,600 absolute).

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[1] By von Kahlden's method.

[2] Compare similar results obtained experimentally by Rosenqvist ("Blutgiftanämien," Helsingfors, 1900.

[3] Stengel: Univ. Penn. Med. Bull., February, 1903.

There may be no definite evidence of hæmolysis or anæmia, and the only symptoms may be cyanosis and general weakness. In a chronic case which I have recently reported[2] the red cells varied between 5,000,000 and 6,090,000 with from 16,000 to 29,800 leucocytes. Methæmoglobin bands were present on spectroscopic examination and the blood in gross was chocolate-brown. The differential count showed a simple polynuclear leucocytosis (83 to 92 per cent); the eosinophiles were always diminished, sometimes absent. The red cells showed a good deal of basophilic stippling and very slight poikilocytosis, but no other peculiarities. There was no demonstrable hæmolysis.

4. *Phenacetin poisoning* (Kronig: *Berl. klin. Woch.*, 1895) may cause actual blood destruction with anæmia in case the patient survives the immediate effects of the deprivation of oxygen. Similar accidents have occurred with phenocol and lactophenin (3 gm. per day—Grawitz).

5. Workers in aniline dyes and nitroglycerin factories may be severely poisoned by *nitrobenzol* compounds inhaled and producing methæmoglobinæmia.

6. *Pyrogallic acid and pyrogallol* as used in treatment of skin diseases may lead to death through destruction of the red cells. Chromic acid (for instance, as applied through the vagina) may have a similar effect.

Many other less common substances work the same ill effects on the blood.

III. SUBSTANCES INJURING THE FUNCTION OF THE RED CELLS WITHOUT PRODUCING HÆMOLYSIS OR METHÆMOGLOBINÆMIA.

The substances in this group, of which *carbonic oxide gas* is the type, poison by combining chemically with the hæmoglobin and preventing its combination with the oxygen of the air.

Illuminating gas is for our purposes the most important.

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[1] T. R. Brown: Internat. Clinics, vol. iv., 12th series.

[2] Cabot: Phil. Med. Jour., November 29th, 1902.

The appearance of individual blood cells is not altered nor do they break up, but the corpuscles are useless to breathe with, as they cannot take up oxygen.

The color of the blood is very *bright* red, much brighter than normal. Spectroscopic examination shows absorption bands of carbonyl-hæmoglobin which are characteristic if not reduced by ammonium sulphide. Their position in the spectrum is very close to that of the oxyhæmoglobin bands and without the chemical test mistakes may occur (Yarrow).[1]

Red Cells.

Von Limbeck[2] found in two cases 6,630,000 and 5,700,000 respectively. The *volume* of these corpuscles (estimated by Bleibtreu's method) was greatly increased, amounting to 70.7 per cent (normal, 41–48 per cent), so that apparently the size of the individual cells is increased.

Münzer and Palma[3] found 5,700,000 red cells in one case.

In a chronic case reported by Yarrow (*loc. cit.*) there was anæmia (3,700,000 red cells) with a moderate leucocytosis and 8 per cent of myelocytes. The other leucocytes were present in normal percentages.

Ehrlich found numerous normoblasts in one case, though no anæmia was present. The presence of normoblasts and myelocytes under these conditions points to a stimulation of the bone marrow, possibly to make up for some hæmolysis of which we have no direct evidence.

Leucocytes.

Eaton[4] reported four cases, in all of which the white cells were increased, the counts ranging between 15,000 and 22,000 per cubic millimetre. Da Costa's case had 32,000 leucocytes with 92 per cent polynuclears and 1.5 per cent myelocytes (480 absolute).

Münzer and Palma (*loc. cit.*) found 13,300 in their case.

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[1] Yarrow: American Med., August 30th, 1903.

[2] *Loc. cit.*, p. 234.

[3] Zeit. f. Heilk., vol. xv., p. 1.

[4] Boston Medical and Surgical Journal, March 14th, 1895.

Twenty-eight such cases have been examined at the Massachusetts General Hospital with the following results:

TABLE LXXXIV.—ILLUMINATING GAS POISONING.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	41	M.	....	31,200	..	Coma; recovery.
2	49	M.	....	27,100	..	September 12th; coma.
				19,900	..	September 13th, entirely well.
3	21	M.	....	26,000	70	Coma; recovery.
4	45	..	....	25,600	100	Death.
5	19	M.	....	25,470	97	
6	50	..	....	25,200		
7	40	M.	....	22,900	75	
				21,200	..	November 27th; coma.
				15,500	..	November 29th; convalescent.
8	Adult	..	....	22,000	..	Recovery.
9	60	M.	....	20,400	75	Coma; recovery.
10	25	M.	....	20,360	100	Death.
11	45	M.	....	20,100	..	Coma; death.
12	Adult	..	....	20,000		
13	64	..	....	19,600	80	
14	24	.	....	18,800		
15	16	F.	....	18,500	84	Coma; recovery.
16	27	..	....	18,100		
17	50	..	....	17,300	90	Temperature, 101°; recovery.
18	22	..	....	17,100		
19	19	M.	....	17,000	..	December 22d.
				17,500	..	December 23d.
			4,930,000	17,000		
20	56	..	....	15,600		
21	21	..	....	15,000	80	
22	19	..	....	13,400	65	
23	55	..	....	12,000	60	
24	28	..	....	9,400		
25	33	..	....	9,300	73	
26	19	..	....	8,600	85	
27	20	..	....	6,700	58	
28	25	..	....	5,000	100	

Warthen[1] reports the same condition in a single case. Here the specific gravity was also very high (v. Limbeck finds that this is to be explained by the increase in the actual size of the corpuscles).

Other poisons of this class are *sulphated hydrogen* (H_2S) and the *cyanide* compounds.

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[1] Virchow's Archiv, vol. cxxxvi.

GENERAL INTOXICATIONS.

I insert here some scattered data on the condition of the blood in general systemic or local corrosive poisoning not primarily or directly affecting the blood itself.

Tansy Poisoning.—A single case examined at the Massachusetts General Hospital showed: Red cells, 4,600,000; white cells, 21,000; hæmoglobin, 70 per cent.

Corrosive Poisoning (Ammonia Fumes).—A patient whose throat was covered with a fibrinous pseudo-membrane in consequence of inhaling ammonia fumes showed a leucocytosis of 25,800. Red cells and hæmoglobin normal. Another with vomiting and purging gave a count of 20,700 white cells.

TABLE LXXXV.—AMMONIA.

Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
24	..	....	27,000	......	Mouth and pneumonia.

Opium Poisoning (Chronic).—The majority of cases of the morphine habit show normal blood, but in October, 1897, a man of twenty-six entered the Massachusetts General Hospital for the morphine habit who showed at entrance 36,000 leucocytes per cubic millimetre. Five days later the count was 21,200. A differential count of 500 leucocytes made on this day showed: Polymorphonuclear neutrophiles, 71 per cent; small lymphocytes, 12; large lymphocytes, 10; eosinophiles, 6; myelocytes, 1. At the time of leaving the hospital he still showed a leucocytosis of 16,400. He had no fever, and the physical examination was entirely negative.

Other cases are tabulated below:

TABLE LXXXVI.—OPIUM.

Acute Poisoning.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	35	....	18,000	95	Morphine ten grains.
2	26	....	16,000	70	Temp. 99.9°; laudanum one ounce.
3	27	....	13,200	95	Opium; melancholia.
4	32	....	13,000	?	Temp. 101.6°; laudanum.
5	21	....	12,000	95	Laudanum.
6	20	......	10,000	90	
7	62	....	4,800	90	

Chronic Poisoning.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	63	....	18,200	75	
2	31	....	13,300	80	
3	36	....	12,800	95	

TABLE LXXXVII.—POISONING, ACUTE.

Chloral.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	19	....	16,800	100	
2	..	....	14,400	54	

Caustic Potash.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	22 mos.	....	27,600	90	July 6th.
			17,000	..	July 8th.
			22,000	..	July 11th.

Corrosive Sublimate.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	64	....	27,200	100	October 6th.
			16,200	..	October 12th.
			21,600	..	October 13th.
			54,600	..	October 14th.
			42,400	..	October 15th. Autopsy.

Belladonna.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	48	....	17,000	95	

Nitric Acid.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
	36	....	12,000	90	
	30	... .	30,200	100	

Smoke Suffocation.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	22	....	23,800	75	November 5th.
			8,000	..	November 6th.
2	75	....	19,100	89	Temperature 99.5°.
3	36	....	19,000	95	Temperature 99.9°.
4	42	4,924,000	16,500	45	
5	12	....	13,000	63	
6	30	....	10,500	70	
7	42	....	8,600	67	

Ptomaïn Poisoning (Rotten Fish).—A mother and her four children were brought to the Massachusetts General Hospital suffering from the effects of decayed fish eaten that day. The blood showed the following: (1) Mother: leucocytes, 21,600, of which 95.3 per cent were polymorphonuclear; (2) boy of seven years: leucocytes, 19,900; (3) boy of three years: leucocytes, 56,800, of which 92 per cent were polymorphonuclear; (4) girl of five years: leucocytes, 32,600; (5) girl of thirteen months: leucocytes, 55,400. The red cells and hæmoglobin were normal. All the patients made prompt recoveries.

TABLE LXXXVIII.—CORROSIVE POISONING.

Carbolic Acid.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	29	..	....	26,400	85	
2	27	..	....	10,800	....	No signs.
3	23	..	....	15,200		

Arsenic.

1	66	..	....	11,600		
2	27	..	....	14,000	80	March 17th.
				18,000	..	March 20th.
				20,000	..	March 23d.
				21,500	..	March 26th.
3	20	..	....	16,000	75	
4	10	..	....	24,200	75	July 3d.
				10,200	..	July 10th.

ACUTE ALCOHOLISM.

Pieraccini (*loc. cit.*, p. 229) in three cases of alcoholic coma records the following differential counts:

Case.	Polynuclears.	Lymphocytes.	Eosinophiles.
1	61.8 per cent.	36.5 per cent.	1.7 per cent.
2	88.4 "	10.8 "	.8 "
3	59.7 "	30.6 "	9.7 "

Achard and Loeper (*loc. cit.*) in four cases of acute alcoholism found "leucocytosis with polynucleosis"; in twenty chronic cases nothing abnormal.

It has been shown experimentally that in animals made drunk with alcohol, there is an invasion of the blood and tissues by micro-organisms from the intestine. It may be that some of the counts here recorded are thus to be explained.

TABLE LXXXIX.—ACUTE ALCOHOLISM.

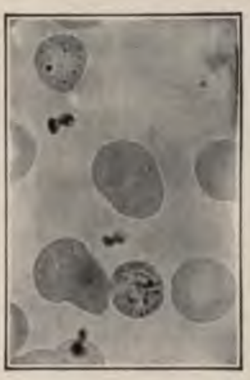
No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	31	..	....	44,000	95	November 1st.
				32,000	..	November 2d.
				20,000	..	November 3d.
2	27	..	....	42,000	..	Followed by delirium tremens.
3	50	..	....	29,800		
				25,000	..	Delirium tremens. Autopsy.
4	35	..	....	23,900		
5	31	..	....	22,000	80	April 27th.
				10,200	..	April 28th.
6	59	..	....	20,900	75	Death.
7	43	..	....	18,200	75	
8	32	..	....	16,200	90	
9	36	F.	....	15,900	..	Two weeks drinking hard; temperature 102°; died, delirium tremens.
10	36	..	....	14,400	95	Delirium tremens; death.
11	38	M.	....	14,200	74	Temperature 101°.
12	43	..	....	14,100	80	
13	42	M.	....	12,000	62	Temperature 101°; delirium tremens.
14	42	..	....	12,600	..	Chronic case of delirium tremens.
15	60	..	....	12,600	75	
16	27	..	....	12,000	90	
17	27	..	....	12,900	65	
18	35	..	....	11,200	95	
19	38	..	....	11,000	85	
20	25	..	....	11,000	80	
21	46	..	....	11,000		
				10,200	..	Delirium tremens.
22	43	..	....	10,400	85	
23	32	M.	3,936,000	10,200	30?	
24	44	M.	....	9,600	80	
				8,100		
25	48	..	....	9,200	95	
26	48	..	....	8,500	90	
27	60	..	....	8,000	80	
28	29	F.	4,288,000	8,000	55	Delirium tremens.
29	37	M.	....	7,800	62	
30	60	F.	....	7,450	65	
				7,000	..	December 21st.
				11,900	..	December 26th.
				6,800		
				6,400	..	Delirium tremens.
31	30	..	....	7,000	80	
32	32	M.	....	5,700	68	Autopsy.
33	28	M.	....	5,600	..	Delirium tremens.
				5,600		

BASOPHILIC GRANULATION OF RED CELLS IN LEAD POISONING.

PLATE G

STAINED WITH WRIGHT'S MODIFICATION OF LEISCHMANN'S STAIN.

(Microphotographs by Lewis A. Brown, Clinico-Pathological Laboratory, Mass. General Hospital.)



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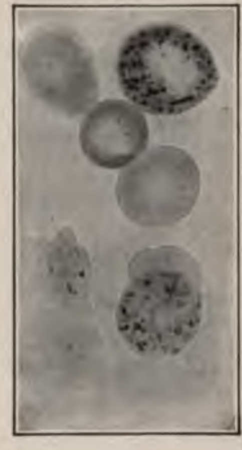

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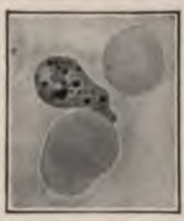

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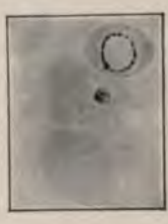

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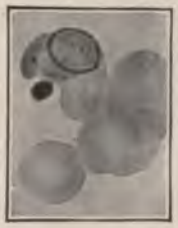

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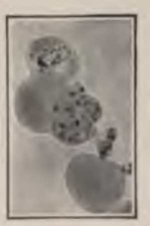

No. 6.

1, 2, and 3, Basophilic stippling.
4, 5, and 6, Ring bodies as seen in anæmic blood.

TABLE XC.—CHRONIC ALCOHOLISM.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	44	..	....	15,500	80	
2	30	..	....	14,200	75	
3	37	..	....	9,000	100	
4	28	..	2,668,000	9,000	60	
5	46	..	....	8,100	80	
7	60	..	....	8,000	80	
8	24	..	....	7,200	80	
9	32	..	....	7,000	95	

MERCURIAL POISONING.

Achard and Loeper (*loc. cit.*) in 2 cases (one with symptoms chiefly digestive, the other cutaneous) found leucocytosis with terminal eosinophilia (8 to 12 per cent). Of 3 cases of chronic mercurial poisoning, 2 showed leucopenia with diminished polynuclears, while in the third the conditions were reversed. In an erythema due to calomel Bezançon (*Arch. gén. de Méd.*, 1902, p. 743) noted eosinophilia (8 to 14 per cent) (see below, page 508).

PLUMBISM.

Among the deleterious effects produced by lead in the human body, anæmia is one of the most serious. It is of the type of ordinary symptomatic anæmias except in one particular, to which attention has recently been called by Grawitz, viz., spotting or stippling of the red cells with fine basophilic granules, which can be well seen in smears stained by Wright's method (*vide supra*, page 41), or any basic dyes. These basophilic granules are often seen in various forms of very severe anæmia, but in plumbism they appear *even when the anæmia and other symptoms are of a mild type* or are absent altogether.

The following table exemplifies the degree of anæmia and leucocytosis ordinarily seen:

TABLE XCI.—LEAD POISONING.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	29	..	4,500,000	23,400	50	Lead colic and headache.
2	30	..	3,800,000	22,800	48	
				16,800	..	Eighth day.

TABLE XCI.—LEAD POISONING (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
3	38	..	....	22,700	64	
4	29	..	....	21,000	75	
5	21	..	5,180,000	14,800	59	
6	40	..	....	14,600	..	December 28th.
				11,400	..	February 2d. Polynuclear, 71.2 per cent; lymphocytes, 24.6; eosinophiles, 4; myelocytes, 2.
7	21	..	....	12,600	72	
8	28	..	....	11,700	65	
9	44	..	3,888,000	11,600	38	Fits, colic, anæmia.
10	39	..	....	11,000	70	
11	35	..	3,700,000	10,000	50	Colic.
12	17	..	3,820,000	9,200	48	Chronic.
13	33	.	4,258,000	8,600	55	
14	32	..	3,208,000	7,200	50	
15	52	..	4,221,000	7,100	45	August 10th. Polynuclear, 72.4 per cent; lymphocytes, 23.3; eosinophiles, 2.5; myelocytes, 1.8; megaloblasts, 1; normoblasts, 1.
			4,848,000	8,000	50	August 20th. Polynuclear, 71.4 per cent; lymphocytes, 25.6; eosinophiles, 2.6; myelocytes, 4; normoblasts, 1.
16	33	..	4,000,000	5,200	50	
17	44	..	3,056,000	5,200	45	
18	37	..	....	4,800	100	
19	40	..	....	4,500		

L. N. Boston (*Phil. Med. Jour.*, September 27th, 1902) has called attention especially to the *leucocytosis* which occurs in plumbism. He presents the following data:

No.	Red cells.	White cells.	Per cent hæmoglobin.	Per cent polynuclears.	Per cent lymphocytes.	Per cent large lymphocytes.	Per cent eosinophiles.	Per cent myelocytes.	Normoblasts.	Megaloblasts.	Remarks.
1	3,335,000	14,000	60	68.5	16.5	10.5	0.5	4.0	1	1	400 whites counted; colic; blue line.
	3,100,000	15,200	68	64.5	20.5	10.5	3.0	1.5	..	..	Eighteen days later.
2	2,930,000	8,000	50	62.5	26.5	8.0	2.5	2.5	4	10	400 whites counted; colic; blue line; paralysis.
3	4,940,000	20,800	87	88.5	7.5	2.0	.0	2.0	0	0	Paralysis; blue line; died twenty-four hours later.
4	5,500,000	11,200	79	71.5	21.5	6.0	1.0	.0	0	0	Colic; blue line.
5	3,810,000	13,200	32	65.5	21.0	9.0	3.0	1.0	0	0	Delirium; blue line; tremor.
6	5,090,000	7,200	37	48.0	40.0	8.5	2.5	1.0	0	2	400 whites counted; colic (mild).
7	3,700,000	7,000	37	63.0	28.5	6.5	.0	2.0	4	1	200 whites counted; no symptoms.
8	2,770,000	4,000	51	60.0	30.0	5.5	.5	4.0	4	0	400 whites counted; debility; blue line.
9	4,760,000	25,500	46	58.0	33.0	4.7	1.0	3.28	4	1	400 whites counted.

During the colic various writers (*e.g.*, Becker[1]) have noted leucocytosis—19,000 or more.

SUNSTROKE AND HEAT EXHAUSTION.

The leucocyte count may be either high or normal, according to conditions not well understood.

TABLE XCII.—SUNSTROKE.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	10	....	24,000	67	
			18,400	..	Two days later.
2	35	....	22,800	..	Temp. 107°. Died.
3	45	....	21,000		
4	46	....	19,400	98	Temp. 109°.
5	60	....	14,800	88	Temp. 106°.
6	49	....	18,600	70	Temp. 110°. Delirium tremens.
7	48	....	18,000	70	Temp. 110.5°. Delirium tremens. Death.
8	64	....	11,500	70	Temp. 109°.
9	23	....	10,000	..	Temp. 110°, first day.
			5,200	..	Temp. 104°, fourth day. Died.
10	47	....	10,000	95	
11	50	....	10,000		
12	32	....	9,800	62	
13	44	....	9,200	95	Temp. 105°. Delirium tremens. Death.
14	30	....	9,000	?	Temp. 108°.
15	28	....	8,200	62	Temp. 107°. Delirium tremens. Death.

Lambert (Loomis-Thompson "System of Med.," vol. iii., p. 876) found in 12 cases of sunstroke hæmoglobin values from 85 to 125 per cent, and a leucocytosis.

Lewis and Packard (*Am. Jour. Med. Sciences*, 1902, p. 406) examined 17 cases of sunstroke. "All but 3 of the severe cases had a leucocytosis at some time, but there was considerable irregularity in the time and duration of the rise. The increase was usually in the polynuclear cells" (94.8 per cent, 89.2 per cent) with absence of eosinophiles.

TABLE XCIII.—HEAT EXHAUSTION.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	..	....	24,000	80	Recovery.
2	20	....	19,800	95	
3	62	....	18,200	..	Recovery. Temperature 98.8°.

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[1] Becker: Deut. med. Woch., September 6th, 1900.

TABLE XCIII.—HEAT EXHAUSTION (*Continued*).

Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
....	11,000	75	Recovery.
....	9,000	..	Recovery. Temperature 98°.
	5,000		
....	8,800	85	Recovery. Temperature 99°.
....	7,600	90	Temperature 97°.
....	6,200	95	
....	5,400	80	Temperature 96°.
....	5,000	85	
....	5,400	73	
....	4,450	61	Temperature 99.6.°

ELECTRIC SHOCK.

Age.	White cells.
25	8,900

PART VI.

MALIGNANT DISEASE, BLOOD PARASITES, AND INTESTINAL PARASITES.

CHAPTER X.

MALIGNANT DISEASE.

The Blood as a Whole.

1. The specific gravity is reduced in most cases, running roughly parallel with the hæmoglobin.

2. Coagulation is normal or slower than normal in uncomplicated cases. When sloughing and inflammation are present it may be rapid.

3. Fibrin is usually normal; an increase means inflammation in or around the tumor or an inflammatory complication.

4. Occasionally the resistance of the red cells is extraordinarily low. In one of my cases the ordinary manipulations of preparing specimens (either fresh or film) for examination invariably mangled the red cells beyond recognition, no matter how quickly and carefully the technique was carried out. In the fresh specimen the red cells seemed to fuse into each other in clumps, their biconcavity lost. The plasma became turbid with hæmoglobin despite every precaution.

This was a case of cancer of the kidney with multiple hemorrhage from various surfaces. I have never seen another case like this one, but in literature several such are mentioned.

CANCER.

Red Corpuscles.

As in tuberculosis, we are frequently surprised to find but little diminution in the number of red cells. In all but very advanced cases this is the rule. It is a change of the individual red cells (pallor, loss of size, of weight, degenerative changes), rather than a reduction of numbers.

Nevertheless in the later cachectic stages of most cases of malignant disease, we do find a quantitative anæmia, the counts often running as low as 2,500,000 and occasionally sinking as low as in pernicious anæmia. Thus v. Limbeck records a case (complicated by repeated hemorrhages) with only 950,000 red cells per cubic millimetre, and Frese[1] cases with 800,000 and 681,000 respectively. The lowest count in my own cases was 1,457,000.

There seems to be no considerable difference between cancer and sarcoma as regards their effects on the red cells.

The count of red cells is sometimes above normal, doubtless due to concentration of the blood from some cause. Probably the same influence is at work in other cases, and many of those showing normal counts have really fewer red cells than they should. Such abnormally high counts are not rare, as the following examples show:

Author.	Case.	Affection.	Red cells.	Per cent hæmoglobin.
Osterspey[2]...	1	Cancer of the stomach.........	5,040,000	80
Osterspey....	2	Cancer of the liver and stomach	6,184,000	87
Osterspey....	3	Cancer of the gullet	8,280,000	48
Neubert[3]	1	Cancer of the stomach.........	5,085,000	73
Neubert.....	2	Cancer of the liver	4,918,000	70
Reinert[4].....		Cancer of the stomach	6,200,000	77

I wish to lay some stress upon this point, because it has been stated by some recent writers (*e.g.*, Grawitz: "Pathologie des Blutes," Berlin, 1896) that the red cells are almost always diminished in malignant disease.

The high counts in cancer of the gullet are obviously to be explained by the lack of liquid taken, the blood being greatly concentrated as in any other form of starvation.

That this increase is not invariably present (see Table XCVIII., page 439) is doubtless because some œsophageal tumors permit the ingestion of liquid in normal amounts and of a certain amount of solids. In gastric cancer high counts are usually due to concentration of the blood produced by vomiting or to the lack of absorption of fluid accumulating in a dilated stomach with pyloric obstruction.

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[1] Frese: Deutsch. Arch. f. klin. Med., vol. 68.

[2] Dissert., Berlin, 1892.

[3] Inaug.-Dissert., Dorpat, 1889.

[4] "Zahlung d. Blutkörp.," Leipzig, 1891.

The highest counts in the Massachusetts General Hospital series are in simple gastric cancer without any stenosis at either end of the organs, and the lowest count (1,632,000) was in a similar case just before death.

Hæmoglobin.

Bierfreund,[1] who has examined 72 cases with regard to their percentage of coloring matter, found that in relatively slow and long-standing cases it averaged 68.5 per cent, and in the worst cases 57.5 per cent. In cases of mammary cancer after operation the hæmoglobin is of course lower owing to hemorrhage, and Bierfreund noticed that as a rule the hæmoglobin began to rise toward normal much later than after operations for non-malignant conditions—a week later on the average—*and that it never reached the point at which it was before the operation.*[2]

The following table from Bierfreund is of interest as illustrating these points. Cases were examined before and after operation, and the examinations were continued daily after the operation until the hæmoglobin began to rise again. This occurred very late as compared with other operations.

Diagnosis.	Per cent hæmoglobin before operation.	Per cent hæmoglobin after operation.	Per cent loss.	Regeneration time.
Malignant tumor without complication.	68.5	53	15.5	23 days.
Very large or rapidly growing tumors.	56.6	38.4	18.2	27.8 days.
Tumors with "softening" or disturbances of function.	57.5	39.7	17.8	27 days.
Total, 72 cases.	Av., 60	Av., 42.8	17.2	Av., 25.9 days.

By "regeneration time" is meant the number of days elapsed after operation before the hæmoglobin *begins to rise.* After operations for other causes (non-malignant) the average regeneration time is from fourteen to twenty days.

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[1] Langenbeck's Archiv, vol. xli.

[2] This is all the more extraordinary because Bierfreund specially noted that even in patients who gained weight notably after the operation the hæmoglobin did not rise so high as it had been before operation; he watched them for months after it. Apparently the actual presence of the tumors is not the only cause of the lack of corpuscle substance.

important that these results of Bierfreund's should be . In likuliez's surgical clinic at Breslau all patients have r hæmoglobin tested regularly. Osler and McCrae in 52 cases astric cancer record an average of 49.9 per cent of hæmoglobin olor index of 0.63. Their readings were:

	Cases.		Cases.
0 per cent or more	3	40 to 50	8
0 to 80	7	30 " 40	14
" 70	6	20 " 30	7
" 60	5	Below 20	[illegible]

Reinbach[1] examined 16 cases and found the hæmoglobin range en 18 to 70 per cent, with an average of 50 per cent.

der's[2] cases average 53 per cent (sarcoma much lower—see).

ker[3] noticed the low hæmoglobin percentage in malignant s and thought it a help in excluding benign tumors or tubers, in which the hæmoglobin is much less diminished.

the 87 cases of malignant tumors in which I have notes of emoglobin (see tables) the average is 58 per cent. Comparing with the average count of red cells (4,140,000), we get a color index of 0.65, distinctly higher than the average of chlorotic cases, of which, however, the figures distinctly remind us. The highest cases of this series had 100 per cent and 90 per cent of hæmoglobin respectively, and the lowest 20 per cent and 22 per cent; in these last two cases the color indexes were 0.36 and 0.58 respectively, not excessively low. As pointed out by Taylor (*loc. cit.*), cases of malignant disease can be divided into three groups with reference to their blood

1. Those with approximately normal blood.
2. Those with a low hæmoglobin but a nearly normal number of cells
3. Those with great diminution both in cells and coloring matter.

Among our own cases at the Massachusetts General Hospital about one-half fall under the second group, one-quarter under the first, and one-quarter under the third.

As the disease progresses, the red cells and hæmoglobin steadily go down (except in cancer of the gullet), and at the time of death

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[1] Langenbeck's Archiv, 1893, p. 486.

[2] "Beiträge z. Kenntniss d. Leucocytosis," Leipzig, 1892 (Vogel).

[3] Wien. med. Woch., 1886, Nos. 18 and 19.

1,000,000 cells per cubic millimetre is not rare. It is very rare to find the red cells reduced below 1,000,000, much rarer than in pernicious anæmia. Improvement under treatment is rare in cancer, common in pernicious anæmia. This is important in diagnosis.

The color index usually remains below 1. Compared to most other varieties of secondary anæmia (*e.g.*, those in tuberculosis or nephritis), a quantitative anæmia—that is, a loss of red cells as well as of hæmoglobin—is relatively more frequent. In general the degree of anæmia is parallel to the amount of cachexia, except when hemorrhage increases it (as in tumors of the stomach or uterus).

How far the anæmia may be due to actual destruction of cells by toxic (?) products of the tumors is doubtful. Grawitz found that the injection of extracts of cancerous tissues caused in rabbits a temporary dilution of the blood, so that the cells per cubic millimetre were diminished, and it may be that this plays some part in the causation of the low blood counts.

Qualitative Changes.

(*a*) *The average diameter of the red cells* is often diminished either as in chlorosis by a diminution in the size of nearly every corpuscle, or by a less general shrinkage, many cells being of normal size. The very large forms seen in pernicious anæmia are rare in the anæmia of malignant disease, and never, I think, reach the size of the giant forms seen in the former condition. Very small cells, on the other hand, are as common in advanced cases as in any other form of anæmia, except chlorosis. Deformities and degenerative changes are very common in well-marked cases, often as great as in pernicious anæmia, though they may be slight or absent.

According to Strauer, the *deformities* found in malignant disease are greater than those found in any form of tuberculosis, and this fact he thinks of value in diagnosis. This observation has been confirmed by Taylor.

Degenerative changes are sometimes well marked, but seldom, if ever, reach so extreme a condition as occurs in many cases of pernicious anæmia.

(*b*) *Nucleated red corpuscles* are the rule in all advanced cases, and in some others. Taylor found them in one-half of the twenty-two cases examined by him. Malignant disease differs in this respect from tuberculosis and most other conditions involving secondary anæmia, in that the nucleated red cells are much more common in cancer and may appear even when there is no considerable loss of red cells (numerically) or even when the hæmoglobin is also normal (Schreiber). I have found them in four-fifths of all severe cases examined.

As a rule the nucleated corpuscles are of the normoblast types (including small forms with dividing nuclei), but in very cachectic cases we may find megaloblasts as well—always, so far as I know, fewer in number than the normoblasts. Osler and McCrae found no typical megaloblasts in their 59 cases. The megaloblasts, when present, are in the minority as compared with the normoblasts. For example:

Case I.	Five normoblasts Three megaloblasts.	Seen while counting 400 leucocytes.
Case II.	Two normoblasts No megaloblasts.	Seen while counting 500 cells.
Case III.	Five normoblasts. No megaloblasts.	Seen while counting 200 cells.

Cases could easily be multiplied.

The characteristics of the blood changes in malignant disease, then, so far as concerns the red cells, are those of secondary anæmia, which at times attains the severest type—but only when cachexia is marked or when hemorrhage complicates the disease.

The specific gravity follows in a general way the hæmoglobin percentage.

On the *white corpuscles* in malignant disease a great deal of interest has centred, and very conflicting reports have been published. As the effects of cancer and sarcoma seem to be somewhat different, we will consider them separately.

THE LEUCOCYTES IN CANCER.

Quantitative Changes.

We should expect great differences in the blood of different cases if we consider what a wide range is included between the small, hard, slow-growing, curable cancer of the lip which may produce little or no impairment of the general health, and the "fulminating," rapidly growing cases with numerous metastases and profound prostration.

The former class of cases may show a blood normal in all respects, while in the latter the blood may be so profoundly altered as to be confused with that of pernicious anæmia or of leukæmia Da Costa found leucocytosis in forty-five per cent of cancer cases and sixty-five per cent of sarcoma cases.

In a general way it may be said that the more "malignant" the cases the greater the changes in the blood.

The effect upon the leucocytes depends upon the following conditions:

1. The position of the tumor.
2. Its size, rapidity of growth, and the number, size, and position of its metastases.
3. The resisting power of the individual.

1. *Position.*—(*a*) Tumors of the gullet involving stricture but not extending to other tissues are often accompanied by a *diminution* of the leucocyte count, owing to the starvation which they produce. This is not true of all cases, as is shown in the accompanying tables, but when the leucocytes are *increased* there is usually an involvement of other organs as well.

(*b*) Cancers of the uterus and some of those of the stomach, by reason of the hemorrhage which they produce, are apt to be associated with a very high leucocyte count.

(*c*) Tumors of the thyroid and of the pancreas are said by some writers to cause a specially great leucocytosis. In my own experience, tumors of the kidney have shown very marked increase of white cells.

2. *Size.*—Other things being equal, the larger and more rapidly growing tumors show in most cases a greater leucocytosis than small, slow-growing ones.

Thus the cancers of the lip and of the pylorus, scirrhus of the breast or of the penis, show smaller counts than tumors of the liver, omentum, and kidney, which are apt to grow more rapidly Metastases in the bone marrow are thought by some observers to give peculiar qualitative blood changes (see below).

In general, metastases, being a method of rapid growth, simply add to the leucocyte count.

These distinctions eliminate some of the apparent contradictions between the findings of different individuals who were simply describing cancers of different types. But even within a single type, there are very marked differences in different cases. For instance, Alexander[1] found the leucocyte count in cases of scirrhus of the breast to vary between 2,360 and 21,700. Similar differences have been reported in cancers of the stomach (*e.g.*, Schneider[2] finding leucocytosis in all of twelve cases, while Osterspey[3] in another series of twelve cases found leucocytosis in only two).

3. *Resisting Power.*—Possibly a part of these differences is to be explained by differences in the resisting power of the individual. But if this is so, we cannot measure the endurance of a given patient by his general health. As in the Civil War the pale, city-bred men outlasted the healthy farmers, so here the tumor's rapidity of growth seems often to be greatest in the most vigorous young individuals, while dried-up old women will resist its advance for a longer period.

We come now to the conditions to be found in particular types of cancerous growth.

Surprisingly little work has been done on the blood in malignant disease, such cases usually being under the charge of surgeons who rarely value such investigations. Except for scattered counts here and there, all our knowledge of the corpuscles rests on the work of Hayem and Alexander in France, and Rieder, v. Limbeck, Pée, Sadler, Reinbach, Osterspey, Grawitz, Strauer, Schneyer, and Schneider in Germany, Cunliffe in England, Da Costa, Taylor, and myself in this country.

Cunliffe's thorough study of seventy-eight cases of cancer (*Medical Chronicle*, September, 1903) is summarized in the table on the opposite page. I regret that it came to me too late to be more fully utilized in this edition.

Da Costa summarizes his results in the following table:

Seat of Growth.	No. of cases.	No. and per cent with leucocytosis.	Average count.	Maximum count.	Minimum count.
Stomach	23	9 or 39	8,100	14,000	1,000
Uterus	10	2 or 20	9,300	24,000	4,500
Rectum	8	4 or 50	10,700	16,000	6,000
Breast	7	5 or 71	14,400	31,500	8,000
Liver	6	4 or 66	18,700	40,800	8,000

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[1] Alexander: Thèse de Paris, 1887.

[2] Inaug.-Dissert., Berlin, 1888.

[3] Inaug.-Dissert., Berlin, 1892.

Location.	No. of cases.	Red Cells.			Hæmoglobin per cent.			Normoblasts.	Leucocytes.			Polynuclears per cent.	Lymphocytes.	Eosinophiles.
		Highest count.	Lowest count.	Average count.	Highest.	Lowest.	Average.		Highest count.	Lowest count.	Average count.			
Stomach. .	10	5,900,000	2,620,000	4,741,000	94	32	71	3 cases	36,800	5,200	17,280	92, 86, 91, 84, 77, 74		
Gullet. . . .	13	6,280,000	3,500,000	4,823,000	115	54	81	1 case	39,800	10,000	13,700	Increased in 11 of 13 cases. Over 80 per cent in 4 cases.	. . . .	5 per cent in 1 case
Rectum . .	10	5,280,000	3,130,000	4,386,000	76	24	57	2 cases	20,200	6,800	12,780	82, 81, 80, 78 Others not increased.	Increased in two cases despite leucocytosis.	
Tongue . .	12	6,070,000	3,790,000	4,940,000	96	60	74	1 case	24,800	7,800	13,400	Increased in 9 of 12 cases.		
Breast. . . .	18	5,550,000	5,330,000	4,560,000	. . .	. .	70	2 cases	35,400	5,400	11,400	7 of 8 with leucocytosis showed increase of polynuclears.		
Uterus . . .	8	4,890,000	2,530,000	4,030,000	72	26	49	2 cases	59,200	7,000	22,800	Increased in 7 of 8 cases.	. . . .	9.8 per cent in 1 case
Abdomen .	7	. . . .	. . . .	3,907,000	. . .	. .	48	. . . . . .	. . . . . .	. . . . . .	9,400	Increased in 4 of 7 cases (86, 81, 74, 74).		
Total .	78													

CANCER OF THE BREAST.

Most of our data came from Hayem[1] and his pupil Alexander.[2]

1. *Scirrhus Growths.*—Number of cases, 14. Average leucocyte count, 11,400. Highest count, 21,700; lowest, 2,360—the last is somewhat doubtful as to diagnosis; except for this case, which was in a very old, dried-up woman, the lowest count was 7,400.

In 10 out of the 14 cases, the count was over 10,000. In the 3 cases seen by the writer 2 showed no leucocytosis, 1 a considerable leucocytosis.

2. *Medullary (Encephaloid) Growths.*—Three cases, all over 10,000—average 11,300.

Houston (*Brit. Med. Journ.*, November 14th, 1903) reports a case of cancer of the breast complicated by many hemorrhages from mucous membranes and under the skin. Repeated blood examinations showed figures like the following: Red cells, 1,600,000; hæmoglobin, 33 per cent (color index, 1.03); leucocytes, 6,000.

Differential count of 500 leucocytes showed: Polynuclears, 56.4 per cent; lymphocytes, 38.3; large mononuclears, 5.2; eosinophiles, 0.

Twenty-seven megaloblasts and thirteen normoblasts were found during this count. At autopsy metastatic cancerous nodes were found in the marrow. The blood, as will be seen, is that of pernicious anæmia.

Effects of Operation.

The following figures from Hayem are also of interest:

CASE I.—Scirrhus of the Breast.

Before operation	21,700	
Five weeks after operation (wound not quite healed)	10,000	
Wound completely healed	6,200	
Seven months after operation	8,990	(beginning to rise again).

The growth recurred some months later and leucocytosis was again present.

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[1] Hayem: "Du Sang," Paris, 1889, p. 947.

[2] G. Alexander: "De la Leucocytosis dans les Cancers," Paris Thesis, 1887.

Case II.—Scirrhus of the Breast.

	First count.	Second count.
Before operation	11,500	11,450
After operation	8,500	6,200

Case III.—Scirrhus of the Breast.

	First count.	Second count.
Before operation	11,000	12,400
After operation	8,400	

Case IV.—Scirrhus of the Breast.

Before operation	7,400
After operation	1,300

Case V.—Medullary Cancer of the Breast.

Before operation	10,000
After operation	9,000

Hayem considers that by watching the leucocyte count we can predict the coming of a recurrence before any physical signs are present. This he did in Case I. of the series just given.

I have seen no confirmation or refutation of this statement. It is one of the many points to which the attention of surgeons should be directed.

CANCER OF THE STOMACH.

Taking all the cases of cancer in my series together, *the average of the 129 at the time when treatment began was 4,018,000 red cells per cubic millimetre.*

In Osler and McCrae's 59 cases the average red count was 3,712,186 per cubic millimetre. Their counts ranged:

Over 6,000,000	3 cases.
5,000,000 to 6,000,000	7 "
4,000,000 " 6,000,000	17 "
3.000,000 " 4,000,000	16 "
2,000,000 " 3,000,000	8 "
1,000,000 " 2,000,000	8 "

Table XCIV.—Gastric Cancer at the Massachusetts Hospital.

Red cells.	
Between 1,000,000 and 2,000,000	6 cases.
" 2,000,000 " 3,000,000	20 "

Red cells.

een 3,000,000 and 4,000,000	44	cases
" 4,000,000 " 5,000,000	32	"
" 5,000,000 " 6,000,000	23	"
Over 6,000,000	4	"
Average, 4,000,000 –	129	cases.

ucleated red cells present in 11 cases out of 114 examined. Normoblasts ys in majority. A few megaloblasts in 3 cases.

TABLE XCV.—GASTRIC CANCER.

Leucocytes per cubic millimetre.

Between 3,000 and 4,000	3	cases
" 4,000 " 5,000	12	"
" 5,000 " 6,000	26	"
" 6,000 " 7,000	26	"
" 7,000 " 8,000	19	"
" 8,000 " 9,000	20	"
" 9,000 " 10,000	26	"
" 10,000 " 12,000	34	"
" 12,000 " 15,000	27	"
" 15,000 " 20,000	28	"
" 20,000 " 30,000	9	"
" 30,000 " 40,000	5	"

Total, 372 counts in 235 cases.[1]

Average, 10,600 +

Hayem[2] in 12 cases found leucocytosis present in 5, absent in 7.

Schneider[3] in 12 cases found leucocytosis in 12 (all).

Schneyer[4] in 18 cases found leucocytosis in 4, and these 4 all under 11,000.

Osterspey[5] in 12 cases found leucocytosis in 5.

Rieder[5] in 6 cases found leucocytosis in 3.

Sadler[6] in 13 cases found leucocytosis in 2, and in both there were complications (abscess of liver, perforation of gullet with gangrene) to which the leucocytosis might be due.

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[1] Where several counts were made in one case they are here averaged and counted as one case.

[2] "Du Sang," Paris, 1889, p. 948.

[3] Inaug.-Dissert., Berlin, 1888.

[4] Inaug.-Dissert., Berlin, 1892.

[5] *Loc. cit.*

[6] "Original-Mittheilungen aus der Klinik v. Jaksch." 1891.

Reinbach[1] in 4 cases found leucocytosis in 2.

Reinert[2] in 2 cases found leucocytosis in 2.

Laache[3] in 5 cases found leucocytosis in none.[4]

Despite these facts we have the record of a certain number of single cases in which the leucocytosis has been enormous For instance, Welch in Pepper's "System of Medicine" mentioned a case in which the ratio of white to red cells was 1: 25 (normally 1:750±).

Eisenlohr's[5] case showed 1 white to 50 red, and Potain's[6] case showed 1 white to 48 red cells.

The Massachusetts General Hospital series of 235 cases showed leucocytosis in 69 cases and none in 176 (see Table XCV.) Out of those showing leucocytosis 27 were under 15,000, that is, the leucocytes were but slightly increased, leaving only 42 out of 235 (or 18 per cent) in which the leucocytosis was very marked. Among these 20, the highest counts were 40,000 and 39,000, and the highest ratio 1:62.

From this series I have excluded all cases in which there was evidence of metastasis in other organs; this means excluding 19 cases, 11 of which showed leucocytosis, and helps to account for the low average leucocyte count in the other 235 cases.

In over three-fourths of these cases the diagnosis was made certain either by operation or by autopsy; all the others showed either a palpable tumor in old cachectic patients with pain and vomiting, or other equally clear evidence for the diagnosis. Doubtful cases have been excluded. As will be seen by the table, in some of the cases the counts were verified by repeated examinations, while in others only a single count—that made when the patient entered the hospital—was recorded.

As a rule, the high leucocyte counts were in the more cachectic cases; but this does not always hold. Three cases in Table XCIV. were very cachectic but showed no leucocytosis

The position of the tumor in one or another part of the stomach seemed to have no connection with the number of leucocytes. Osler and McCrae[1] found no leucocytosis in 29 cases out of 62. Their counts showed:

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[1] Langenbeck's Archiv, 1893, p. 486.

[2] *Loc. cit.*

[3] "Die Anämie," Christiania, 1883.

[4] Apparently, since he draws attention to the fact that there is leucocytosis in a case of cancer of the uterus.

[5] Deut. Arch. f. klin. Med., 1877, vol. xx.

[6] Gaz. des Hôp., 1888, No. 57.

Leucocytes.	
Below 5,000	14 cases.
5,000 to 8,000	15 "
8,000 " 12,000	15 "
12,000 " 20,000	15 "
20,000 " 30,000	3 "
	62 cases.

Their highest count, 28,000, was in a case with extensive hepatic metastasis. The number seemed to bear no fixed relation to the situation of the growth, nor to the amount of ulceration, of metastasis, or of fever.

On the whole we get, I think, very little information of any diagnostic value from blood counts in gastric cancer. Leucocytosis is relatively infrequent in cancer of the stomach, occurring in only about one-fifth of the early cases. As the disease progresses we may get a leucocytosis, particularly in case its growth is *rapid* and metastastes are frequent and numerous; but some cases, particularly those in which the tumor is small and grows slowly, may run their entire course without any leucocytosis being present. In this respect they are like the majority of small, slow-growing cancers in other parts of the body (see below).

Hemorrhage or perforation is of course accompanied by an increase in the number of white cells—in fact the highest count in the present series (105,600) occurred in a case in which a cancer of the stomach with metastases in the liver perforated into the peritoneal cavity and started a virulent, quickly fatal peritonitis.

DIGESTION LEUCOCYTOSIS IN CANCER OF THE STOMACH.

A considerable body of statistics has accumulated to show that in the great majority of cases of gastric cancer the leucocytosis of digestion (see page 91) does not occur. R. Müller[2] noticed this fact in 5 cases of cancer of the stomach. Schneyer[3] in 18 cases found it invariably absent, while in 3 cases of benign stenosis of the pylorus a considerable digestion leucocytosis appeared, as was also the case in 7 out of 8 cases of ulcer of the stomach, the exception being a fatal case.

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[1] Osler and McCrae: N. Y. Med. Jour., May 19th, 1900.

[2] Prag. med. Woch., 1890, No. 17.

[3] Zeit. f. klin. Med., 1895, p. 475.

He found both incipient and advanced cases to be similarly affected. In 5 of his cases and in some of Müller's HCl was present in the gastric contents, so that the absence of digestion leucocytosis was not due to absence of HCl.

Hartung[1] in a series of 10 cases (mostly advanced) found no digestion leucocytosis, whereas a marked increase occurred in cases of malignant disease of other organs. Osler and McCrae found no digestion leucocytosis in 12 out of 22 cases.

Capps[2] in 17 cases examined at the Massachusetts General Hospital found a digestion leucocytosis in 2, the increase being respectively 3,270 and 3,850 cells over the count before the beginning of digestion. In the other 15 cases there was no increase after a large proteid meal. Since Dr. Capps' article 20 more cases have been investigated at the hospital, in 19 of which the digestion leucocytosis was absent. Thus in a *total of 37 cases only 3, or 8 per cent, showed any digestion leucocytosis.* In 5 out of 10 cases of chronic gastric catarrh the digestion leucocytosis was present; it was also present in a case of benign stricture of the pylorus in a man of forty-nine on whom an operation was successfully performed later. The digestion leucocytosis may, however, be absent in various gastric diseases and in simple debility and has been shown by Renki[3] and others to be subjected to the normal function of the pylorus and of the bowels. Out of 144 cases tabulated from various authors by Da Costa, 119, or 82 per cent, had no digestion leucocytosis.

On the whole subject of the blood in gastric cancer I agree in the main with the conclusions of Osler and McCrae (*loc. cit.*):

"1. In a doubtful case a blood count below 1,000,000 red cells per cubic millimetre is strongly in favor of pernicious anæmia.

"2. While nucleated red corpuscles occur in all very severe anæmias, megaloblasts rarely if ever appear in cancer of the stomach.

"3. Neither an increase in the leucocytes nor special variation in the different forms appears to be of any moment in the diagnosis of gastric cancer.

"4. The presence or absence of digestion leucocytosis is too uncertain to be of much assistance in diagnosis."

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[1] Wiener klin. Woch., p. 697, 1895.

[2] Boston Med. and Surg. Journal, November 4th, 1897.

[3] Renki: Arch. f. Verdauungskr., 1901, vol. vii.

CANCER OF THE STOMACH WITH METASTASES.

st writers have not separated the cases with metastasis from without it. A glance at the nineteen cases of Table XCVI. s that with four exceptions leucocytosis was present throughout of the disease.

TABLE XCVI.—CANCER OF THE STOMACH WITH METASTASES.

		Sex.	Red cells.	White cells.		Remarks.
		..	5,539,000	3,900 a.c.	35	Polynuclear, 65 per cent; lymphocytes, 32; eosinophiles, 3.
				4,200 p.c.	..	
			4,228,000	5,000	70	January 23d. Stomach and liver.
				6,200	..	January 28th, mealtime.
				7,300	..	January 28th, three hours later.
		M.	....	7,000	70	February 14th, no cachexia.
			5,168,030	14,400	62	March 6th, liver involved.
				19,600	..	March 12th.
				21,640	..	March 17th, cachectic.
	6	..	....	8,000	85	Operated.
				8,500 a.c.		
				7,600 p.c.		
5	45	..	3,536,000	8,100	60	
6	23	..	3,120,000	9,000	20	Operation.
				19,000	.	Two weeks later. Died.
7	37	..	....	9,600	80	+ Omentum.
8	41	..	4,273,000	10,000	57	Stomach, liver, and glands.
9	38	M.	5,432,000	10,190	52	January 6th. Stomach and liver.
				13,653	..	January 12th.
						January 22d. Died.
10	47	..	4,424,000	11,200	50	+ Gall bladder.
11	48	..	....	12,800	45	+ Liver.
12	41	..	....	14,000	75	+ Liver. February 25th.
				14,800 a.c.	..	February 27th.
				15,600 p.c.		
18	60	..	....	15,000	60	+ Liver.
14	36	..	....	15,600	85	+ Liver.
				14,300		
15	Adult	M.	3,352,000	16,000	..	Stomach, liver, and spleen.
16	44	..	4,128,000	17,100	40	+ Liver.
17	29	..	5,104,000	21,000	72	+ Omentum.
18	54	M.	4,160,000	24,000	60	Stomach and liver.
				24,200		
				22,500		
19	47	M.	....	34,350	..	November 7th, cancer of stomach and liver.
				30,600	..	November 11th.
				105,600!	..	November 14th, Perforation peritonitis.

The variations in the following case are of interest:

Table XCVII.—Cancer of Stomach with many Metastases.

Age.	Date.	Red cells.	White cells.	Per cent hæmoglobin.	Per cent polynuclear.	Per cent small lymphocytes.	Per cent large lymphocytes.	Per cent eosinophiles.	Achromia.	Erythroblasts.	Remarks.
48	Dec. 20th.	4,816,000	13,600	75	62.0	23.0	13.0	2.0	Much	None	No variation in size.
	Dec. 30th.	....	5,800	65							
	Jan. 3d.	....	8,000								
	Jan. 6th.	4,832,000	5,600	55							
	Jan. 8th.	....	......	..	64.0	26.0	8.0	2.0	Some	None	No variation in size.
	Jan. 9th	5,224,000	7,200	60							
	Jan. 30th.	....	......	55							
	Feb. 2d.	5,360,000									
	Feb. 10th.	4,096,000	6,200	45	76.0	15.0	8.5	.5	Some	......	Little variation in size and shape. Little polychromatophilia.
	Feb. 14th.	....	15,200	..							
	Feb. 28th.	2,496,000	9,300	35	78.5	20.0	1.0	.5	Some	......	No great variation in size or shape. No polychromatophilia.
	Mar. 18th.	1,944,000	3,600	20	67.3	23.7	8.5	.5	Some	None	
	Mar. 28th.	1,784,000	4,800	10	76.0	16.5	3.5	2.0	Some	None	Myelocytes two per cent. Some poikilocytosis. Microcytes. Autopsy.
	April 8th.	1,152,000	3,200	8							

CANCER OF THE GULLET.

Most authors are agreed that *no increase*—in fact usually a decrease—of white cells is the rule in this disease. Thus Rieder found 6,900 in one case; Osterspey's two cases showed no leucocytosis, and Escherich and Pée found similar results.[1] This is probably due to the fact that the position of the tumor, by causing starvation, tends to lower the leucocytes, while it belongs to a class of small, slow-growing cancers which do not as a rule tend to produce leucocytosis.

Nevertheless, 12 of the 26 cases in the Massachusetts General Hospital series (see Table XCVIII.) *did* have leucocytosis, perhaps owing to some metastasis or complication.

Table XCVIII.—Cancer of the Gullet.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	32	..	....	5,400		
2	68	..	....	5,800	60	
3	59	..	....	6,000	70	
4	50	..	....	6,400		
5	58	M.	3,488,000	6,800	100	May 11th.

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[1] Reinbach's two cases showed a diminution in the polymorphonuclear cells, which in all probability means a normal or diminished leucocyte count.

LE XCVIII.—CANCER OF THE GULLET (*Continued*).

			Red cells.	White cells.	Per cent hæmo-globin.	Remarks.
				6,800	..	May 18th.
		..	....	6,800	50	
		F.	....	7,000	..	October 18th.
				10,600		
				5,400	..	October 19th, before food.
				6,600	..	October 19th, after food.
				9,860	..	October 20th.
		..	4,044,000	7,000	60	December 29th.
				13,750	..	January 31st.
				14,400	..	February 25th.
			....	7,000 a.c.		
				6,900 p.c.		
			..	7,500	60	
			00	7,600	50	Before food.
			.	11,500	..	Four hours later.
			....	7,700	75	
			....	8,200	90	
			4,920,000	8,725	72	
			....	11,100	68	
			... ...	10,300		
			... .	11,800		
		M.	....	11,800	30	Hæmaturia also.
		..	6,624,000	11,900	90	Vomiting.
		..	....	13,000	80	January 14th.
				14,000	..	January 21st.
20	47	..	....	13,700	70	
21	47	M.	....	15,400	80	
22	38	M.	....	15,600	60	
23	67	M.	4,604,000	16,400	60	During digestion.
24	64	..	....	16,400	65	
25	38	..	4,560,000	20,600		
26	47	..	....	38,000	80	January 20th.
				82,000	..	January 30th. Autopsy.

CANCER OF THE LIVER.

(See Table XCIX.)

Wlajew[1] records a case in which the red cells fell to **850,000** with 1.020 specific gravity.

Of our 53 cases, leucocytosis was present in 29—over one-half, others showing a leucocytosis later—a larger proportion than in gastric cancer. The cases were not all primary in the liver or bile ducts, but none originated in the stomach, and in all the greater part of the growth was in the liver itself.

The comparatively great diminution in the red corpuscles will

[1] Wlajew: St. Petersburg. med. Woch., 1894, No. 48.

be noted in the Table XCIX. The condition both of red and white cells is doubtless due to the rapid growth of tumors of the liver as compared, *e.g.*, with those of the stomach or lip (see below).

TABLE XCIX.—CANCER OF THE LIVER.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	35	..	1,680,000	4,800	20	August 3d.
			2,128,000	......	20	August 7th.
			1,840,000	......	20	August 12th.
			2,968,000	10,200	30	August 19th.
			2,612,000	8,100	30	August 26th.
2	55	M.	4,170,000	5,000	..	Bile ducts = starting-point. Autopsy.
3	61	M.	3,824,000	5,200	52	
4	42	..	....	6,200	..	Autopsy.
5	52	..	5,100,000	6,800	80	Bile ducts.
6	59	..	....	7,400		
7	58	..	....	7,600	90	
8	43	..	4,060,000	7,800	30	
9	44	F.	4,968,000	7,800	69	January 4th, 1896. Autopsy.
			3,784,000	19,700	68	February 12th, 1896.
10	59	M.	4,570,000	8,000	..	Operated.
11	31	F.	4.572,000	8,000	62	
12	59		....	8,300	63	
13	46	..	....	8,500	..	Gall bladder.
14	43	..	4,212,000	8,700	50	
15	72	M.	4,100,000	9,000		
16	50		....	9,000 a.c.	..	Bile ducts.
				10,400 p.c.		
17	52	..	....	9,100	75	
				9,100 a.c. 8,500 p.c.		
18	54	M.	4,072,000	9,300	..	Diff., 1,000 cells: Poly., 82.4 per cent.; small lymph., 8.5; large lymph., 8.1; old lymph., 1.
19	42	..	5,600,000	9,600	66	Gall bladder.
20	35	M.	3,800,000	12,500 9,800 22,000	.. .. ..	November 3d November 5th November 6th Poly., 92 per cent.; lymph., 8. Autopsy.
21	44	..	3,732,000	9,800	40	December 5th. Poly., 75 per cent; lymph., 22; eosinophiles, 3; reds, pale centres.
				20.000 a.c. 18,800 p.c.	..	December 21st.
22	..	M.	4,108,000	9,970	45	January 1st, 1896.
				11,200	..	January 3d, 1896. Autopsy.
23	67	..	4,176,000	10,200	55	
24	65	M.	....	10,300	58	
25	57	..	3,856,000	10,400	30	Poly., 68 per cent.; lymph., 30; eosinophiles, 2.
				11,400 a.c. 16,600 p.c.		
26	40		....	10,400	60	Operated.
27	50	M.	3,200,000	10,800	..	Primary in bile ducts. Autopsy.

TABLE XCIX.—CANCER OF THE LIVER (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent haemo-globin.	Remarks.
28	49	..	....	10,800	80	
29	53	..	4,456,000	11,000	65	April 3d.
			4,032,000	....	68	April 21st.
30	64	..	... ...	11,200	..	April 20th. Bile ducts and gall stones.
				12,650 a.c.	..	April 26th.
				14,750 p.c.		
31	57	M.	....	11,150	50	
32	69	..	....	11,800	50	
33	47	..	....	12,200	65	
34	70	..	....	13,000	..	January 20th. Jaundiced.
				28,400	..	January 28th. Died January 30th.
35	33	..	....	13,600		
36	48	..	....	14,000	60	
37	43	M.	4,160,000	14,100	..	July 17th. Autopsy, July 19th.
38	56	..	3,956,000	14,200	47	Poly., 84 per cent; lymph., 15.6; eosinophiles 4.
				14,900 a.c.		January 17th. Gall stones.
				17,800 p.c.		
			5,120,000	....	65	January 24th.
39	52	..	....	15,500	70	
40	52	.	4,400,000	15,600	75	
	64	M.	2,768,000	15,800	45	May 6th.
			2,880,000	21,900	..	May 24th.
				1,530	45	May 28th.
			2,928,000	11,700	..	June 8th.
41	31	..	....	15,700	80	February 27th.
				13,100	..	February 28th.
42	30	F.	3,660,000	17,200	82	Poly., 83 per cent; myelocyte, 1.
				16,800		
43	48	..	2,900,000	17,500	48	Poly., 92 per cent; lymph. 5.8; eosinophile, 1; myelocytes, 2. Autopsy.
44	63	..	3,864,000	17,600	55	
45	31	M.	3,130,000	18,700	52	December 20th.
				15,600	..	December 30th. Before food.
				14,000	..	December 30th. Four hours later.
46	37	..	....	20,600		
				19,000 a.c.		
				20,000 p.c.		
47	66	..	3,704,000	21,000	50	
48	58	..	....	23,200	..	January 31st.
				22,200	..	February 12th. Abscess of liver.
49	45	..	....	24,400	..	March 14th
				17,200	70	
50	Adult	M.	4,408,000	25,500	70	
51	65	..	....	27,000	70	April 12th.
				17,000	..	April 14th.
				13,000	..	April 16th. Diff. count 500 cells: Poly., 85.6 per cent; small lymph., 11.6; large lymph., 2.8.

TABLE XCIX.—CANCER OF THE LIVER (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
52	46	..	2,824,000	32,600	83	Omental hernia. Purpura hæmorrhagica. Internal hemorrhage. Poly., 84.8 per cent; lymph. 15.2; eosinophiles, 0; no nucleated reds; considerable variation in size; moderate poikilocytosis.
53	50	M.	4,544,000	35,600	..	November 29th, 1895.
				36,400	..	December 10th, 1895.
			3,136,000	28,000	.	January 15th, 1896.
			4,056,000	28,000	..	February 16th, 1896. Autopsy.

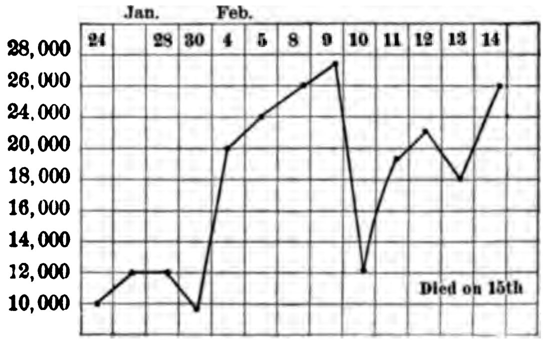

FIG. 31.—Chart of Leucocytes in a Case of Cancer of the Liver.

CANCER OF THE INTESTINE.

The leucocyte counts range both high and low.

Hayem[1] found cancer of the rectum to show only 9,500 leucocytes. Reinbach[2] found in three cases of cancer of the rectum moderate leucocytosis.[3] Only 15 of the 39 cases in our series (see Table C.) showed leucocytosis, and in one of these there was a complicating pylephlebitis which probably raised the count.

The red cells show little change.

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[1] *Loc. cit.* [2] *Loc cit.*

[3] Apparently—that is, the percentage of polynuclear cells was increased. He did not count the leucocytes as a whole.

TABLE C.—CANCER OF THE INTESTINE.

No.	Age.	Sex.	Red cells.	White cells.	Per ct. hæmoglobin.	Remarks.
1	28	M.	....	5,300	72	Cancer of cæcum. Operation.
2	59	F.	4,800,000	5,500	33	Cancer of cæcum. Autopsy
3	33	M.	4,368,000	5,800	83	Cancer of colon. Operated.
4	41	F.	5,560,000	5,800	45	Cancer of cæcum operated successfully.
5	59	..	....	6,000	33	December 7th.
			3,452,000	....	40	December 9th Polynuclear, 65.6 per cent; lymphocytes, 31.4; eosinophiles, 3.
			3,840,000	11,700	40	December 21st.
6	62	..	....	6,400 a.c. 10,000 p.c.	..	Hepatic flexure.
7	28	..	....	6,600	84	Hepatic flexure.
8	66	M.	4,268,000	7,150	78	Cancer of intestine (where?).
9	38	..	....	7,200	85	Sigmoid
10	23	..	....	7,200	90	Rectum.
11	59	..	....	7,400	70	Splenic flexure.
12	52	M.	....	7,400	55	Metastases, primary in sigmoid.
13	..	..	3,504,000	7,400 a.c. 8,300 p.c.	50 ..	Hepatic flexure. Polynuclear, 80 per cent; lymphocytes, 19; eosinophile, 1.
14	39	..	... ...	7,500		
15	52	M.	2,424,000	7.800	..	Cancer of cæcum. No digestion leucocytosis.
			2,440,000	6,800	..	
16	50	..	....	7,800		
17	50	..	....	8,600	90	Rectum.
18	31	M.	4,921,000	8,800	..	Cancer of hepatic flexure. Operated.
19	32	..	....	9,000	75	Sigmoid.
20	47	F.	....	9,300	63	Cancer of cæcum.
21	36	..	3,504,000	9,800	40	Operated.
22	62	..	4,416,000	10,000	65	Hepatic flexure.
23	53	..	4,992,000	10,000	51	Descending colon.
24	34	..	4,524,000	10,800	38	Rectal. Polynuclear, 78 per cent; lymphocytes, 19.8; eosinophiles, 2.2.
25	45	..	3,358,000	11,500	25	Polynuclear, 68 per cent; lymphocytes, 28.5; eosinophiles, 3.5.
26	50	F.	5,416,000	12,000	..	Cancer of Rectum.
27	49	..	4,872,000	12,300	50	Rectum with metastases in liver.
28	56	M.	4,408,000	12,700	60	Cancer of duodenal papilla with pylephlebitis. Autopsy.
29	17	..	....	13,600		
30	53	..	5,960,000	13,700	60	
31	58	..	....	15,000	85	Transverse colon.
32	58	M.	4,160,000	15,200	50	Cancer of rectum. Operation.
33	45	..	....	15,400	70	Rectum.
34	34	M.	....	15,500	40	Metastases, primary in sigmoid.
35	46	..	....	21,600	80	Rectal and omental.
36	58	..	....	24,000	85	Cancer of sigmoid.
37	62	..	....	25,200	75	
38	20	..	....	26,700	98	
39	..	..	2,760,000	....	15	Cancer of cæcum. July 16th.
			2,480,000	... .	15	July 19th.

CANCER OF OMENTUM AND ABDOMINAL ORGANS GENERALLY.

The twenty-three cases seen at the Massachusetts General Hospital in which cancerous tissue was pretty generally distributed through the abdominal organs, all showed leucocytosis with eight exceptions (see Table CI.)

TABLE CI.—CANCER OF OMENTUM AND ABDOMINAL ORGANS GENERALLY.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	50	F.	....	Greatly increased.	Markedly diminished.	Primary in pancreas. Diff. count of 400 cells; Poly., 84.5 per cent; small lymph., 8, large lymph., 5; eosinophiles, 2.5. Autopsy.
2	63	..	5,440,000	5,350	..	Colon.
3	47	..	6,072,000	5,800	65	
4	59	..	.. ....	6,000	35	
			3,452,000	......	40	December 9th. Poly., 65 6 per cent; lymph., 31; eosinophiles, 3; basophiles, 4.
			3,840,000	11,700	40	December 21st.
5	64	..	3,512,000	7,000	62	Bladder.
6	48	M.	....	7,250	..	May 13th.
				6,500 7,300	..	May 20th. No digestion leucocytosis.
7	42	M.	4,560,000	7,800	60	October 13th. Poly., 88 per ct.; lymph., 10; eosinophiles, 2
				10,600	..	October 16th.
8	67	..	....	7,800 a.c. 8,100 p.c.		
9	47	..	....	8,000	65	Cæcum.
				8,300	..	General in abdomen.
10	70	..	....	8,700	60	Gall bladder.
11	26	M.	....	9,000		
12	63	..	2,860,000	10,600	35	Poly., 84 per cent; lymph., 10.2; eosinophiles, 6; myelocytes, 8; normoblasts, 1.
				9,600	..	
13	40	M.	2,208,000	11,500	55	December 13th. Peritoneum.
			1,875,000	15,600	..	December 19th.
						December 13th. Diff. count 400 cells: Poly., 83 per cent; lymph., 16; eosinophiles, 1.
						December 19th. Polynuclear, 80 per cent; lymphocytes, 20. eosinophiles, 0.
14	65	M.	... .	11,700		
15	44	..	....	13,600	68	February 10th.
				14,200	..	February 18th. Peritoneal Autopsy.

TABLE CI.—CANCER OF OMENTUM AND ABDOMINAL ORGANS GENERALLY (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
16	Adult	M.	3,772,000	13,700	..	Autopsy.
17	62	..	3,840,000	14,400	60	November 14th. Abdominal.
				7,800	70	November 23d. Secondary in liver and glands.
						November 14th. Diff. count 400 cells: Poly., 77 per cent; lymph., 22; eosinophiles, 1.
						November 23d. Polynuclear, 69.5 per cent; lymphocytes, 30; eosinophiles, 0.5.
18	28	..	4,496,000	152,000	45	Peritoneal.
			2,995,000	18,000	60	Poly., 79 per cent; lymph., 14.5; eosinophiles, 3.5. Kidney and spleen.
19	46	..	8,000,000	20,400	50	Poly., 88 per cent; lymph., 10; eosinophiles, 2; normoblasts, 16; megaloblasts, 2. Count 500 cells. Size of reds normal.
				12,600	65	
20	60	..	....	25,000	62	
21	Adult	F.	5,500,000	26,200	..	Autopsy.
22	45	F.	....	27,400	..	Questions of aneurism. Autopsy.
23	Adult	M.	....	Greatly increased.	Markedly diminished.	Diff. count of 500 cells: Poly., 80 per cent; lymph., 20.

CANCER OF THE KIDNEY.

Of ten cases which I have examined (see Table CII.) eight showed large leucocyte counts—viz., 12,900, 19,980, 25,000, 27,000, 28,500, 43,100, 82,000, and 91,000. In three of these cases, however, the tumors may have been sarcomata, as no microscopical examination was made. Most of the cases had fever, chills, and signs of inflammation, which may account for part of the leucocytosis.

TABLE CII.—CANCER (OR SARCOMA) OF KIDNEY.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	58	..	3,840,000	7,600	50	
2	48	..	....	8,100	..	Autopsy.
3	76	..	5,046,000	9,100	45	Sarcoma.

TABLE CII.—CANCER (OR SARCOMA) OF KIDNEY (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
				19,980	..	Autopsy.
4	14	..	....	11,600 a.c. 12,900 p.c.	..	March 14th. Polynuclear, 72 per cent.; lymphocytes, 27; eosinophile, 1.
				7,900 a.c. 9,000 p.c.	..	March 17th.
5	..	..	....	23,000	..	Autopsy.
6	53	M.	4,312,000	25,000	32	Differential count of 800 cells: Polynuclear, 80.9 per cent.; lymphocytes, 15.8; eosinophiles, 3.3. No nucleated red cells.
7	2	F.	3,756,000	27,000	..	Differential count of 500 cells: Polynuclear, 66 per cent.; lymphocytes, 29.5; eosinophiles, 2; myelocytes, 2.5; normoblasts, 24; megaloblasts, 2. Autopsy.
8	57	F.	5,200,000	28,500	..	Supposed leukæmia. Differential count of 500 cells: Polynuclear, 81.8 per cent.; small lymphocytes, 12; large lymphocytes, 4.2; eosinophiles, 2. Autopsy.
9	49	F.	3,360,000	43,100	..	Supposed leukæmia. Differential count of 1,000 cells: Polynuclear, 92.9 per cent.; lymphocytes, 6.2; myelocytes, .9; normoblasts, 2; megaloblast, 1. Autopsy.
10	50	F.	4,111,000	82,000	..	July 8th.
			2,780,000	91,000	..	Polynuclear, 98 per cent.; lymphocytes, 2.

Von Limbeck's[1] case mounted steadily from 18,514 to 80,541.

CANCER OF THE UTERUS.

In six cases Hayem[2] found no increase—the counts ranging from 4,575 to 9,500, with an average of 7,800.

Rieder,[3] on the other hand, in a single case found 30,800, and the seven cases counted at the Massachusetts General Hospital showed a leucocytosis in five (see Table CIII.).

There is need of more data on this subject.

TABLE CIII.—CANCER OF THE UTERUS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	35	..	....	6,400	62	
2	45	..	....	8,200	75	
3	42	..	3,716,000	8,200	35	Diff. count 500 cells: Poly., 68 per cent; small lymph., 23; large lymph., 8; eosinophiles, 1.
4	43	..	4,772,000	8,600	43	
5	43	..	....	11,900	70	
6	59	..	....	16,800	.	First day.
				7,400 a.c. 12,000 p.c.	..	Third day.

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[1] *Loc. cit.*

[2] *Loc. cit.*

[3] *Loc. cit.*

TABLE CIII.—CANCER OE THE UTERUS (*Continued*).

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
7	48	F.	2,696,030	19,400	20	October 26th.
			3,232,000	30,700	..	October 28th.
8	51	F.	....	34,900	..	Diff. count of 1,000 cells: Poly., 88 per cent; small lymph., 11.7; eosinophiles, 0.2; myelocytes, 0.1. Two normoblasts.
9	31	F.	2,889,680	22,250		
10	28	F.	....	20,170	75	Ureter blocked: anuria nine days. Autopsy.

TABLE CIV.—CANCER OF THE OVARY.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	50	..	3,532,000	16,400	50	
2	36	F.	4,500,000	25,000	62	Operation.
3	..	F.	3,248,000	32,800	..	Operation.
				CANCER OF THE PROSTATE.		
1	63	..	2,596,000	9,200	35	December 13th.
			2,212,000	11,000	..	December 19th.
						Polynuclear, 74.4 per cent; lymphocytes, 23.6; eosinophiles, 2.
2	45	M.	....	10,200		
3	51	..	....	18,000		
				CANCER OF THE LIP.		
1	51	M.	7,000,000	6,300		
				CANCER OF THE BREAST.		
1	60		....	18,000	..	First day.
				14,000	..	Third day.
2	46		....	15,200	100	
3	57		5,200,000	12,200	68	
4	?	F.	....	Marked increase.	..	Diff. count 400 cells: Poly., 89 per cent; lymphocytes, 11 per cent.
5	41		....	11,900	70	
6	67		....	11,000	85	Recurrent.
7	4		....	9,300	90	
8	44		....	8,500	80	Both breasts.
9	?	F.	....	Not increased.	..	Diff. count of 600 cells; Poly., 72.4 per cent; lymphocytes, 25.4; eosinophiles, 2.2.
10	31	F.	....	8,200		
11	54		....	8,200	65	June 16th.
				12,800	..	July 4th. Death.
12	7		....	8,000	80	January 16th.
				10,500	..	January 25th.
13	63		....	7,600	85	
14	32		....	7,200	85	

CANCER OF THE NECK.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	42	M.	....	Marked increase.	..	Polynuclear, 88.5 per cent.
2	....	..	....	20,000		

METASTATIC GLANDULAR CANCER.

	27		....	38,700	80	February 15th.
				6,900	..	February 21st. Autopsy. Diff. count, 400 cells: February 16th. Poly., 54.4; lymphocytes, 42.7; eosinophiles, 2.9. February 17th. Poly., 66.2; lymphocytes, 30; eosinophiles, 1.8.

CANCER IN ETHMOIDAL CELLS.

	35		6,096,000	27,800	..	July 11th. Diff. count, 400 cells: Poly., 83.5 per cent; lymphocytes, 15.8 per cent; eosinophiles, 0.7 per cent.
				21,500	..	July 23d.
				22,100	..	July 27th.
				17,000	..	July 30th.
				24,000	..	August 1st.
				29,700	..	August 5th.
				20,400	..	August 9th.
				21,400	..	August 12th.
				22,600	..	August 16th.

CANCER OF THE PANCREAS.

1	55	M.	....	18,800	70	Metastases.
2	56	M.	....	17,600	..	Liver and spleen also.
3	64	M.	....	15,900	..	General peritonitis.
4	56	..	....	11,000	75	Head.
5	52	..	....	10,500	65	December 28th.
				14,600	..	January 1st.
				22,000		
6	49	..	....	10,000	80	January 3d.
7	50	..	....	6,100	77	June 17th.
				7,222	..	June 22d.

CANCER OF VERTEBRÆ.

	62	F.	....	13,200		

ADENOMA OF THE SUPRARENAL BODY.

	59	M.	....	24,200	..	Autopsy.

MEDIASTINUM.

1	25	..	....	10,700	70	April 20th Polynuclear, 87 per cent; lymphocytes, 12 per cent; eosinophiles, 1 per cent.
				9,300	..	April 26th
				8,300	..	April 27th
				6,800	..	May 1st
2	47	..	5,008,000	12,800	80	July 7th. Stricture of œsophagus. Larynx.
				14,000	..	July 18th. No autopsy.

SKULL.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	57	..	....	9,200	..	Cerebral.
2	70	..	.. ....	8,600	..	May 7th.
				15,800	..	May 22d.
				14,600	..	May 28th. Metastases.
GENERAL.						
1	63	..	....	14,600	70	
2	..	..	4,700,000	5,000	60	Multiple myeloma. (Wright.)
CANCER OF THE BLADDER.						
	55	..	2,856,000	12,600	42	Papilloma. Diff. count, 500 cells: Polynuclear, 63.4 per cent; small lymphocytes, 29 per cent; large lymphocytes, 6 per cent; eosinophiles, 1.6 per cent.
CANCER OF PLEURA.						
	63	..	....	20,000	65	Endothelioma. Autopsy.

Cancer of the lip has apparently been neglected so far as blood examination is concerned. Hayem, Rieder, and Reinbach give but one case each, the counts being respectively 7,000, 11,600, and "not increased." In a single case at the Massachusetts General Hospital I found 6,300.

The following scattered counts may be added: Cancer of tongue, 7,000 (Hayem); cancer of scrotum, 6,700 (Hayem); cancer of navel, 7,100 (Hayem); cancer of larynx, 7,200 (Hayem), 16,000 (Reinbach); cancer of pancreas: Hayem, 2 cases—9,400 and 9,900; Schneider, 1 case—12,000; cancer of vagina, 9,800 (Rieder); cancer of penis, 7,000 (Hayem); cancer of thyroid, 70,000 (Hayem) a very rapidly growing tumor; cancer of mediastinum, "marked increase" (Reinbach); cancer of prostate,[1] 10,200.

Qualitative Changes in the Leucocytes.

1. The percentage of polymorphonuclear neutrophiles is usually high in cases with leucocytosis and normal in those without it.

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[1] Braun (Wien. med. Woch., 1896, p. 582) mentions a cancer of the prostate in which the leucocytosis, instead of being made up mostly of polynuclear leucocytes, was associated with a large increase of the small lymphocytes together with numerous eosinophilic myelocytes.

This rule holds for perhaps three-fourths of the cases; but there are many exceptions to it. For instance, Taylor[1] reports 27,840 leucocytes with 65.6 per cent polymorphonuclear cells, 14,800 leucocytes with 66.2 per cent polymorphonuclear cells, 25,000 leucocytes with 58.2 per cent polymorphonuclear cells, 45,000 leucocytes with 43.7 per cent polymorphonuclear cells, the last a marked lymphocytosis. On the other hand, he found 88.7 per cent of polymorphonuclear cells in a total leucocyte count of 3,000. My own experience and Cunliffe's is similar—*i.e.*, 88 per cent of polymorphonuclear cells with a total count of 7,800 leucocytes, though I have never seen so marked a lymphocytosis as was present in Taylor's cases. He also noted a relative increase in the large lymphocytes which my counts and those of Cunliffe have not shown. Osler and McCrae found an average of 81 per cent of polymorphonuclear cells in 22 cases, the higher percentages being in the cases with highest total leucocyte count. These writers confirm the observation of Taylor that the large mononuclear and transitional leucocytes are often relatively increased in cancerous disease. Taylor found in 15 cases with leucocytosis an average of 19.3 per cent of these cells and in 6 cases without leucocytosis 26 per cent. Eight of these cases were cancer of the stomach—the remainder cancer of other organs. All were cachectic. Osler and McCrae in 22 cases of gastric cancer record an average of 8.5 per cent of large mononuclear and transitional varieties. They do not agree with Taylor in believing the excess of these cells is sufficient to be of diagnostic value.

Reinbach found in 8 cases with leucocytosis 89 per cent in 2 cases and 87, 86, 83, 81, 80, and 77 per cent in others. Cunliffe (*loc. cit.*) in 86 cases found an average of 73.4 per cent polynuclear. There was marked lymphocytosis in 3 cases. In the Massachusetts General Hospital series the following percentages occurred: When no leucocytosis was present, 88.7, 88, 86, 79, 66, 62.5, 62, 60, 57 per cent, etc. With leucocytosis, 96, 98, 92, 90, 90, 88, 87, 86, 84, 83, 74 per cent, etc. (see Tables XCVI., XCIX., CI., CIII.).

2. *Eosinophiles* are not always notably decreased (as they are in many other leucocytoses), nor are they regularly increased. In Reinbach's 16 cases the average percentage was 2 + per cent. In Osler's 22 cases it was 1.1 per cent. In Cunliffe's 86 cases 1.06 per cent, although 6 cases showed eosinophiles, and the highest (9.8

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[1] Taylor: Internat. Med. Mag., July, 1897.

per cent) in cancer uteri. In the Massachusetts General Hospital cases the average was 1.2 per cent, but in 7 of the 38 cases in which differential counts were made no eosinophiles were seen. Christian (*Am. Med.*, January 24th, 1902) reports a case of enormous cancerous growth in the liver (thirty-three pounds weight). The following counts were recorded nine months before death, and show *marked eosinophilia*.

November 8th, 1900.		November 24th, 1900.	
Red cells	3,704,000	Red cells	3,952,000
White cells	8,600	White cells	9,800
Hæmoglobin	75 per cent.	Hæmoglobin	50 per cent.
Polynuclear	45.5 per cent.	Polynuclear (333)	50.8 per cent.
Lymphocytes	31.5 "	Lymphocytes	38.7 "
Large lymphocytes	9.5 "	Large lymphocytes	38.7 "
Eosinophiles	13.5 ! "	Eosinophiles	10.5 "

3. *Myelocytes.*—Perhaps more commonly than in other conditions except leukæmia and pernicious anæmia, we find in malignant disease small percentages of myelocytes.

About one-half of all the cases of cancer examined by me have shown myelocytes. Cunliffe noted them in 6 cases out of 86.

Epstein[1] in a case of cancer with metastatic bone nodules noticed large numbers of nucleated corpuscles (normoblasts and megaloblasts) and myelocytes, but I think the association was a mere coincidence, since I find that myelocytes and erythroblasts are very commonly present in cachexia with anæmia from any cause.

SARCOMA.

In general the effects of sarcoma are like those of cancer, but *worse*. The literature of the subject is rather scanty.

Red Cells.—Hayem in a case of osteosarcoma counted the red cells at 663,400 per cubic millimetre.

Laker[2] describes an "abdominal cystosarcoma" in which two counts of red cells showed 2,800,000 and 2,500,000.

Von Limbeck[3] in 1 case found 1,118,000, and in another 2,240,000. Both were osteosarcomata.

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[1] Wiener med. Presse, December, 1894.

[2] Wien. med. Woch., 1886, p. 926.

[3] *Loc. cit.*, p. 343.

Sadler[1] in 3 cases found 2,710,000, 3,637,000, and 4,500,000.

Rieder[2] in 3 cases (all osteosarcomata) found 1,846,160, 3,700,000, and 3,995,000.

Da Costa in 14 cases found the red cells ranging from 5,400,000 to 2,510,000 with an average of 3,900,000. The hæmoglobin from 83 to 42 per cent, averaging 63 per cent, and the white cells from 7,000 to 40,000, averaging 13,276. Only 3 of his 14 cases had over 15,000 leucocytes. Cunliffe, in 19 cases affecting various organs, found the highest count 5,150,000, the lowest 2,240,000, the average 4,260,000. The hæmoglobin averaged 62 per cent, color index 0.73. Normoblasts were seen in 2 cases. The leucocytes ranged from 5,400 to 32,000, averaging 14,960. The polynuclears were relatively increased in 18 out of 19 cases. Eosinophiles increased in 2 cases (6 and 9.4 per cent).

The Massachusetts General Hospital blood counts include 22 cases in which the red cells were counted (see Tables CV. and CVI.), the average being 4,500,000, not nearly so low as that recorded by other observers; still low counts occurred (2,706,000, 2,637,000, 3,842,000).

The qualitative changes in the red cells consist (as in cancer) of the "degenerative" changes (deformities in size and shape, englobular changes) present in marked cases, and the presence of nucleated corpuscles, when cachexia is marked.

TABLE CV.—SARCOMA WITH LEUCOCYTOSIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks
1	..	..	4,188,000	98,000	....	Polynuclear cells, 90.2 per cent.
2	41	M.	3,842,000	71,000	55	Sarcoma of lung, etc. Autopsy.
3	21	F.	2,706,000	56,000	....	Sarcoma of kidney. Autopsy.
4	20 mts.	..	4,000,000	44,600	42	Polynuclear cells, 70 per cent.
5	29	..	....	36,000	74	Melanotic sarcoma; perforation of intestine; peritonitis.
6	30	..	4,512,000	26,100	70	Neck.
			5,422,000	28,500	75	One month later. Polynuclear, 89 per cent; lymphocytes, 9.8; eosinophiles, 1.2.
7	..	..	4,312,000	25,000	32	Polynuclear, 80.9 per cent.
8	32	M.	2,630,000	24,000	50	General sarcomatosis.
			2,900,000	21,000	....	One week later. Autopsy.
9	63	..	....	22,000	85	Chest wall. Polynuclear, 76.5 per cent; lymphocytes, 23; eosinophiles, 0.5.

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[1] *Loc. cit.*, pp. 38, 39.

[2] *Loc. cit.*, pp. 98, 100.

ABLE CV.—SARCOMA WITH LEUCOCYTOSIS (*Continued*).

No.	Age	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
		..	....	21,800	75	Testicles. Autopsy.
		..	....	19,980	....	Neck. Autopsy.
		..	5,480,000	18,400	35	December 2d. Adrenal.
				21,600	....	December 5th.
				16,600	40	December 16th.
			....	18,300	80	Rib.
		M.	....	18,000	..	Sarcoma of abdominal organs.
		..	....	17,200	55	Lung. Autopsy.
	35	..	4,560,000	17,000	65	Melanotic sarcoma of all the abdominal organs (bone metastasis?). November 30th, 1895. Diff. count, 600 cells: Polynuclear, 71 per cent; small lymphocytes, 11; large lymphocytes, 5.2; eosinophiles, 12.4 (!); myelocytes, 4.
				23,900	....	December 7th.
				33,400	....	December 13th.
				37,900	....	December 19th.
				41,200		
				33,000	....	December 22d.
				36,000	....	December 26th.
				40,200		January 14th.
				55,400	...	January 28th.
17	46	M.	4,700,000	16,000	....	Sarcoma of abdominal organs.
				19,000	....	Three days later. Autopsy.
18	68	F.	6,200,000	16,000	....	Sarcomatosis.
19	48	M.	....	Marked increase.	....	Diff. count, 700 cells: Polynuclear, 70 per cent; lymphocytes, 22; eosinophile, 1; myelocytes, 7. Sarcomatosis.
20	28	..	....	15,200	80	Sarcoma of intestines.
21	..	..	....	Great increase.	....	Osteosarcoma (thigh). Diff. count, 500 cells: Polynuclear, 74 per cent; small lymphocytes, 19; large lymphocytes, 6; eosinophiles, 1.
22	58	..	....	14,100		Cæcum.
23	34	..	....	14,000	80	Right pubic bone.
24	..	..	....	Great increase.	....	Sarcoma of abdominal organs. Diff. count, 800 cells: Polynuclear, 84 per cent; lymphocytes, 15.5; eosinophiles, 1.2.
25	24	M.	4,352,000	13,600	....	Sarcoma of kidney.
26	..	..	....	13,200	....	Sarcoma of abdominal wall.
27	57	M.	4,180,000	13,000	47	Melanotic sarcoma of abdominal organs.
				16,250	...	
				15,180	....	One week later
28	31	..	....	13,000	95	Adrenal.
29	36	..	....	11,000	85	Uterus.
30	49	..	4,712,000	10,900	60	Left kidney.
31	10	..	....	10,200	70	Abdominal wall.
32	54	..	....	9,800	72	Kidney operated.

Small tumors are often without any effect on the blood (see Table CVI.). According to v. Limbeck[1] this is oftener true than in cancer.

TABLE CVI.—SARCOMA WITHOUT LEUCOCYTOSIS.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	38	..	....	9,500	80	Sarcoma mediastinum; metastasis of spine. Autopsy.
2	37	F.	4,980,000	9,000	78	Sarcoma of ovary.
3	?	M.	4,946,000	9,000	....	Osteosarcoma of shoulder.
4	40	..	....	9,000	75	Liver, secondary.
5	29	M.	5,280,000	8,200	...	Sarcoma of testicle.
6	26	.	4,800,000	8,000	80	Sarcoma of lung. Autopsy
7	44	..	....	7,600	70	Ovary.
8	41	..	... ...	7,400	80	Metastatic liver, secondary.
9	36	M.	....	6,700		
10	58	..	... ...	6,500	....	Cutaneous.
11	46	..	5,390,000	6,100	55	Glands.
12	24	M.	4,952,000	6,000	....	Small recurrent sarcoma of groin.
13	70	..	4,520,000	6,000	70	Multiple small round cell.
14	34	..	....	6,000	78	Recurrent.
15	47	..	4,288,000	5,600	65	Kidney operated.
16	35	..	....	5,100 5,700 a.c. 8,600 p.c.	65	Retroperitoneal. Polynuclear, 66 per cent; lymphocytes, 33.4; eosinophiles, 0.6. Reds good

Hæmoglobin.—Reinbach's[2] 20 cases ranged between 23 and 75 per cent, averaging 52 per cent.

Bierfreud[3] in 29 cases found variations between 40 and 75 per cent.

Von Limbeck's 2 cases had 28 and 48 per cent respectively.

Rieder's[4] 4 cases showed at the beginning of treatment 29, 56, 57, and 65 per cent respectively, but in 1 case the hæmoglobin went down gradually while under observation until it reached 6 per cent (!), the lowest point, Rieder says, that he has ever seen in any disease.

Sadler's[5] cases showed 33, 45, and 78 per cent.

In the 16 cases of Table CVI. in which this point was noted, the average is 59 per cent.

On the whole, the coloring matter seems to be more diminished than in most cases of cancer.

Leucocytes.—The following tables, slightly modified from v. Limbeck, show the important points:

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[1] *Loc. cit.* [2] *Loc. cit.* [3] *Loc. cit.* [4] *Loc. cit.* [5] *Loc. cit.*

No.	Observer.	Diagnosis.	Count.
	Hayem.	Osteosarcoma.	11,250
	Alexander.	“	52,700
	“	“	16,430
	“	“	16,275
	“	“	17,050
	“	“	15,900
	“	“	15,570
	“	“	13,020
	Alexander.	Osteosarcoma.	10,950
	“	“	12,090
	“	“	11,248
	Rieder.	“	12,700
	“	“	10,900
	“	“	9,100
	“	“	8,000
	v. Limbeck.	“	32,000
	“	“	26,800
	Reinbach.	“	20,000
	“	“	13,000
	Mass. General Hospital.	“	21,000
	“ “ “	“	9,000
		Average,	17,000 ±

No.	Observer.	Diagnosis.	Count.
1	Hayem.	Lymphosarcoma.	11,700
2	Alexander.	“	19,910
3	“	“	19,530
4	“	“	11,696
5	“	“	11,470
6	“	“	10,540
7	v. Limbeck.	“	55,100
8	“	“	38,000
9	“	“	10,800
10	Sadler.	“	33,248
11	“	“	19,299
12	“	“	9,044
		Average,	20,000 +

No.	Observer.	Diagnosis.	Count.
1	Rieder.	Melanosarcoma.	41,600
2	“	“	28,500
3	“	“	22,300
4	Reinbach.	“	25,000
5	“	“	8,000
6	Mass. General Hospital.	“	37,900
7	“ “ “	“	13,000
		Average,	25,100 +

CANCER OF OMENTUM AND ABDOMINAL ORGANS GENERALLY.

The twenty-three cases seen at the Massachusetts General Hospital in which cancerous tissue was pretty generally distributed through the abdominal organs, all showed leucocytosis with eight exceptions (see Table CI.)

TABLE CI.—CANCER OF OMENTUM AND ABDOMINAL ORGANS GENERALLY.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	50	F.	....	Greatly increased.	Markedly diminished.	Primary in pancreas. Diff. count of 400 cells: Poly., 84.5 per cent; small lymph., 8, large lymph., 5; eosinophiles, 2.5. Autopsy.
2	63	..	5,440,000	5,350	..	Colon.
3	47	..	6,072,000	5,800	65	
4	59	..	....	6,000	35	
			3,452,000	......	40	December 9th. Poly., 65 6 per cent; lymph., 31; eosinophiles, 3; basophiles, 4.
			3,840,000	11,700	40	December 21st.
5	64	..	3,512,000	7,000	62	Bladder.
6	48	M.	....	7,250	..	May 13th.
				6,500 7,300	..	May 20th. No digestion leucocytosis.
7	42	M.	4,560,000	7,800	60	October 13th. Poly., 88 per ct.; lymph., 10; eosinophiles, 2
				10,600	..	October 16th.
8	67	..	....	7,800 a.c. 8,100 p.c.		
9	47	..	....	8,000	65	Cæcum.
				8,300	..	General in abdomen.
10	70	..	....	8,700	60	Gall bladder.
11	26	M.	....	9,000		
[illegible]	[illegible]3	..	2,860,000	10,600	35	Poly., 84 per cent; lymph., 10.2; eosinophiles, 6; myelocytes, 8; normoblasts, 1.
				9,600	..	
[illegible]	[illegible]	M.	2,208,000	11,500	55	December 13th. Peritoneum.
			1,875,000	15,600	..	December 19th.
						December 13th. Diff. count 400 cells: Poly., 83 per cent; lymph., 16; eosinophiles, 1.
						December 19th. Polynuclear, 80 per cent; lymphocytes, 20. eosinophiles, 0.
[illegible]	[illegible]	[illegible]	... .	11,700		
			[illegible]	13,600	68	February 10th.
				14,200	..	February 18th. Peritoneal Autopsy.

continuing over 40 for several weeks.[1] Autopsy showed sar-
atous nodules in the bone marrow. In another case, a tumor
the abdomen, the eosinophiles were 10.5 per cent, and in two
ers 8 per cent.

A case of apparent sarcoma of the abdominal organs (no autop-
at the Massachusetts General Hospital in January, 1896, had
per cent of eosinophiles.

Such cases should certainly make us think of bone metastases,
Neusser speaks of osteosarcomata as being accompanied by
nophilia, but the evidence is as yet fragmentary.

3. *Myelocytes.*—Reinbach's case just described had a low per-
ige of myelocytes.

The following cases illustrate the same point:

Case I. is a case of sarcomatosis in a man in whom sarcomatous
les were distributed all over the internal organs and in the skin.
ifferential count of 700 white cells showed in his case:

	Per cent.
Typical myelocytes (over 15 μ)	2
Small myelocytes (under 15 μ)	5
Lymphocytes	22
Polynuclear neutrophiles	70
Eosinophiles	1

The autopsy showed no special lesions in the spleen, glands, or bone marrow, except those due to the sarcomatous nodules.

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[1] The full counts are as follows:

April 4th, 1892.		May 20th, 1892.	
Red cells	5,396,000	Red cells	4,512,000
White cells	120,000 (!)	White cells	52,000
Hæmoglobin	60 per cent.	Hæmoglobin	55 per cent.

DIFFERENTIAL COUNTS.

	April 4th.	May 1st.	May 20th.	May 26th.
	Per cent.	Per cent.	Per cent.	Per cent.
Poly. neut.	48	51	55 +	51 +
Eosinophiles	48	46	42	44 +
Lymphocytes	2.7	2.32	1.5	3.2
Myelocytes	1	.68	.64	.8

CASE II.—Sarcoma of the abdominal wall. A differential count of 800 cells showed:

	Per cent.
Polynuclear neutrophiles	84.
Lymphocytes	10.5
Large lymphocytes	5.
Eosinophiles	.2
Myelocytes	.3

CASE III. No. 5, Table CV.—Six hundred cells contained:

	Per cent.
Polynuclear neutrophiles	71.
Lymphocytes	16.2
Eosinophiles	12.4
Myelocytes	.4

Summary of Blood Changes in Malignant Disease.

1. Small, slow-growing tumors and the early stages of all tumors may have no effect on the blood appreciable by our present methods of examination.

2. In advanced cases the red corpuscles often become thin, light, and pale, and finally their number may be greatly decreased, the counts running sometimes as low as in pernicious anæmia. In this respect, as in others, sarcomata seem to injure the blood more than cancers.

3. The color index is always below 1, but is rarely as low as we find it in severe chlorosis.

4. Normoblasts and megaloblasts (the latter being in the minority) may occur, the former even in the absence of severe anæmia. Deformities in size and shape are common.

5. Leucocytosis is present in the cachectic end-stages of many cases, but is frequently absent in small tumors of slow growth and without metastases. The polymorphonuclear cells are often relatively increased.

6. Fibrin is not increased.

Diagnostic Value.

1 When we are dealing with an obscure, deep-seated disease, if hemorrhage is excluded, the presence of persistent leucocytosis suggests suppuration or malignant disease (rather than tuberculosis or syphilis, for example), and excludes any simply functional or hysterical affection. The *absence* of leucocytosis, however, does not

ignant disease, though it makes suppuration very un-

een malignant disease and suppuration—if the other mptoms do not decide—there may be nothing in the ecide. In decided pyæmia we may get pyogenic cocci the od by culture, but a negative result would not exclude rating focus.

nce of any increase of fibrin in the blood speaks against , and therefore in favor of malignant disease; but the f increased fibrin network not decisive either way, as it met with in connection with neoplasms, though more com- in suppuration.

Between malignant disease and hemorrhage a marked anæ- vors the latter, provided the case is a recent one; for the f malignant disease is comparatively slow to develop. The s give no help.

Between cancer and ulcer of the stomach, if there has been ecent hemorrhage, leucocytosis favors cancer; but its *absence* o weight either way.

ne hæmoglobin is said to decrease steadily in cancer, while in ulcer it tends to return toward normal after the cessation of hemorrhage.

The presence and persistence of digestion leucocytosis speak against cancer, and its absence in favor of cancer. It must be remembered, however, that any variety of *catarrh* or *dilatation* (should such be present) can also prevent digestion leucocytosis, and that the latter is not invariably present even in health.

5. Between cancer of the liver or bile ducts on the one hand and *simple* gall-stone colic or gall-stone obstruction on the other, the presence of leucocytosis favors cancer. As usual, however, its absence does not exclude cancer, and we must bear in mind that gall stones *with cholangitis* may raise the leucocyte count as much as cancer. Simple cysts or echinococcus cysts cause no leucocytosis, nor does syphilis of the liver.

6. The appearance in the blood of large numbers of eosinophiles, myelocytes, and nucleated corpuscles during the course of a malignant disease suggests a bone metastasis.

7. When a leucocytosis which has disappeared after removal of a neoplasm reappears, we may expect recurrence of the growth shortly.

8. A steadily increasing leucocytosis in a case of malignant disease points to a rapidly growing tumor or to the occurrence of metastasis.

9. Between malignant disease and pernicious anæmia, the diagnosis rests on the following points:

(*a*) Color index and volume index low in malignant, apt to be high in pernicious anæmia.

(*b*) Leucocytes often increased in malignant, diminished in pernicious anæmia.

(*c*) Lymphocytes often relatively decreased in malignant, increased in pernicious anæmia.

(*d*) Average size of red cells often decreased in malignant, and often increased in pernicious anæmia.

(*e*) If nucleated red corpuscles are present the normoblasts are in a majority in malignant disease, and in a minority in pernicious anæmia.

10. The presence of leucocytosis is against the benignness of any tumor.

11. When no actual increase of leucocytes is present, an increased percentage of the polymorphonuclear variety among those present may have the same significance as a leucocytosis.

CHAPTER XI.

BLOOD PARASITES.

EXAMINATION FOR THE MALARIAL PARASITE AND ITS PRODUCTS.

I. Time for Examination.

It is often stated that the organism is most easily found during the chill. But this is not the writer's experience. During a chill it is often difficult and sometimes impossible to find the organisms. Eight hours before or after a chill is the most favorable time (Thayer), although parasites have been found as late as forty-eight hours after the last chill. During the chill many organisms retire to the internal organs.

The number of organisms varies a great deal. In some cases they are present in every field of a one-twelfth immersion lens, while in others we may find only one after an hour or more of patient search. In some cases of coma Ewing had to search one and two hours before finding a single parasite. In the majority of the cases occurring near Boston, it needs but a few minutes' search to find parasites if the blood be taken within twelve hours before or after a chill, and provided no quinine has been lately given. Occasionally in mild cases the organisms are very scanty; and it may be almost impossible to find any. I agree with Theobald Smith and Ewing that when the parasites are scarce, especially when they are of the small unpigmented form, a prolonged search through fresh blood frequently proves negative, although a few minutes suffices for the discovery of one or more minute parasites in the stained specimen.

II. Method of Examination.

(*a*) *Fresh Blood.*

A slide of fresh blood is prepared as described on pages 6–8 and examined with a one-twelfth immersion lens.[1] Lower powers

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[1] In cold weather both slide and cover should be warmed before using. Indeed this is always well, as it makes the corpuscles spread better.

PARASITES OF TERTIAN FEVER. **PLATE V.**

(WRIGHT'S MODIFICATION OF LEISCHMANN'S STAIN.)

Photographs by Wright & Brown, Clinico-Pathological Laboratory, Mass. General Hospital.

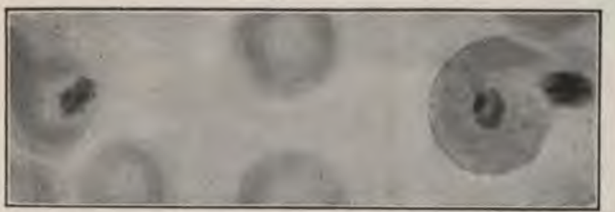

FIG. 1.—The spotted cell on the right is an erythrocyte containing a young tertian organism and overlapped at its margin by a blood-plate. The dark mass overlying the cell at the extreme left is also a blood-plate.

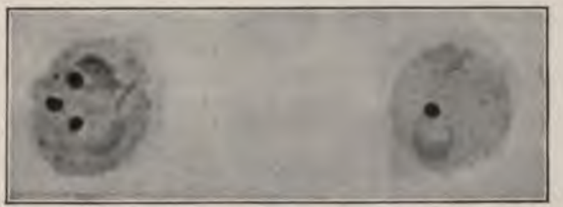

FIG. 2.—Two red cells showing granular degeneration. That on the right contains one, that on the left two, young tertian parasites. The chromatin bodies appear as rounded black spots.

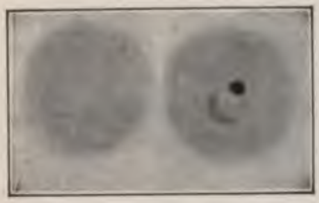

FIG. 3.—Young Tertian Parasite.

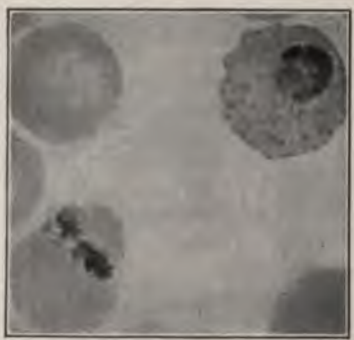

FIG. 4.—Above, a tertian parasite about six hours old. Below, a blood-plate overlying a red cell.

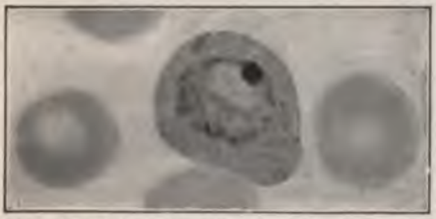

FIG. 5.—Tertian Parasite about ten hours old. In this and in the next figure the granular degeneration of the red cell is very marked.

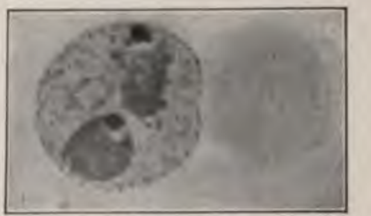

FIG. 6.—Red Cell considerably enlarged, and containing two young tertian parasites.

TERTIAN PARASITES ABOUT HALF GROWN

AND OCCUPYING ENLARGED AND DEGENERATED ERYTHROCYTES. (STAINED AS IN PLATE V.) IN NO. 2 TWO BLOOD-PLATES APPEAR AMONG THE CELLS.

Photographs by Wright & Brown, from the Clinico-Pathological Laboratory, Mass. General Hospital.

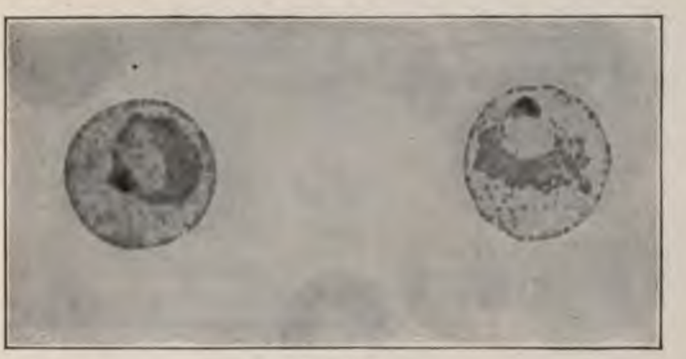

FIG. 1.

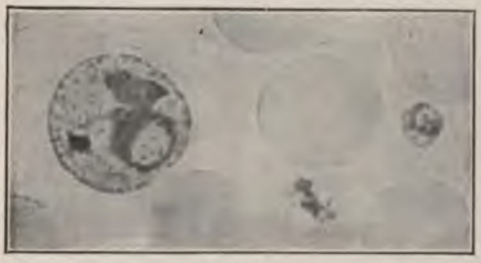

FIG. 2.

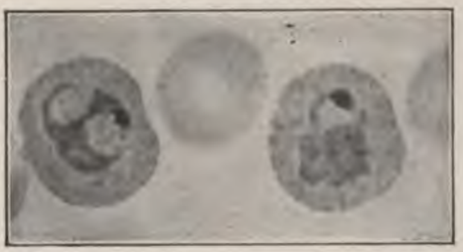

FIG. 3.

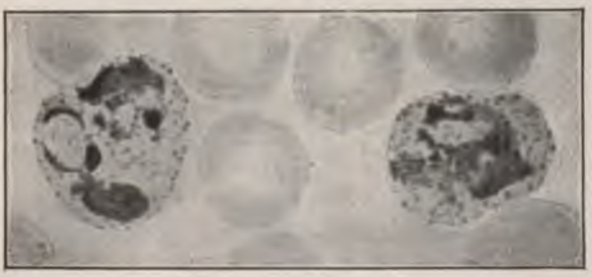

FIG. 4.

should not be used, although in skilful hands they are often sufficient. Portions of the slide in which the corpuscles do not overlie each other should be chosen for examination. As we pass the slide along beneath the lens it is well to be on the lookout for any *specially large* or *specially pale* corpuscle. Such a one will catch the eye if we are on the watch for it, even though the slide is being passed along very rapidly, and all such should be carefully examined.

Another thing to watch for is anything *black or dark brown.* If the slide is not perfectly clean, or if the cover glass has touched the skin in collecting the blood, there will often be black spots which make us pull up short and examine, only to find that they are bits of dirt. This loses time, and hence, as above noted, the importance of care and cleanliness in the earlier stages of the process.

Besides any strikingly pale or swollen corpuscle or any black dots, we should be on the lookout for any *movements* in the field The movements of Müller's "blood-dust" (see page 58) are often mistaken by beginners for those of the malarial organism Their greatly smaller size and extracorpuscular position serve to distinguish them in most cases. I have sometimes thought I saw pigment in these bodies. If, as Stokes believes, the "blood-dust" is derived from the leucocytes, it is possible that they might carry out with them some pigment ingested by the leucocyte

Flagellate bodies may be studied in fresh specimens, if possible, on a warm stage. Usually they appear only after the lapse of from ten to twenty minutes from the larger tertian or ovoid æstivo-autumnal organisms. The addition of a little water or salt solution may facilitate the escape of the parasite from the red cell and the formation of flagella.

Ewing finds that a moist chamber may be secured in a Petri dish with tightly fitting vaselined cover. Wet blotting-paper placed in the dish furnishes the necessary moisture. Specimens spread on slides or covers may be kept moist for ten to twenty minutes in such dishes, and flagellation proceeds with moderate rapidity

A simple method is as follows: Cut an opening one-half by one inch in a piece of thick blotting-paper and moisten the paper in hot water. Spread two glass slides rather thickly with fresh blood, lay the blotting-paper on one slide, cover the cut opening by the other, specimen side down, and slip a rubber band about both. After fifteen or twenty minutes the slides and paper may be separated and the two specimens dried.

alarial Organism.—It practically is never to be seen out-le the corpuscle. Most malarial organisms are to be found within e corpuscle, and *only there.*[1]

For those who have not examined many specimens of malarial ood it is a very difficult thing to find the organism in the early ages of its growth, and the number of mistakes in diagnosis is ery large. I always look with great suspicion on any report of nalarial blood as containing *only* "hyaline forms" in fresh speci-iens.

In the later stages, when the organism has become well pig-nented, there is nothing that at all resembles it, and those who ave seen and watched it a few times can hardly mistake anything lse for it. Not so with the so-called "hyaline" or youngest form the organism. Personally I think the *name* "hyaline bodies" is responsible for a part of the mistakes. We are led to expect omething more shiny and refractile than the organism really is, nd so are misled by the brilliant white circles to be found at the centre of many normal corpuscles under certain conditions of light nd partial drying up. Time and again I have been asked to look at malarial organisms (always the "hyaline" forms), and found nothing more than one of these effects of light which can be found in any normal blood, if the conditions are right.

As soon as the organism gets any pigment (and there are very few times in the cycle of a malarial case when there are not *some* pigmented organisms present), the active rapid motion of the black pigment dots is unlike anything else seen in the blood, and when once recognized can never be forgotten or mistaken. It is only when the pigment has ceased moving (owing to the death of the organism) that the differentiation between dirt and malarial pigment becomes difficult.

Almost all stages of the growth of the plasmodium which we can watch in the blood drawn from the peripheral circulation take place within the corpuscle. It is true that as the pigmented organism gets toward its full growth, and before the granules have begun to gather at the centre, we may find it very difficult to see any trace of corpuscle substance around the margin of the plasmodium. Sometimes we see a ring of non-pigmented glistening white substance outside the moving black dots (see Fig. 2, 7, Plate I.) stand-

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[1] Except degenerate forms, free flagellæ, and spores at the moment of segmentation (*rarely* to be seen). Crescents and ovoid bodies are intracellular.

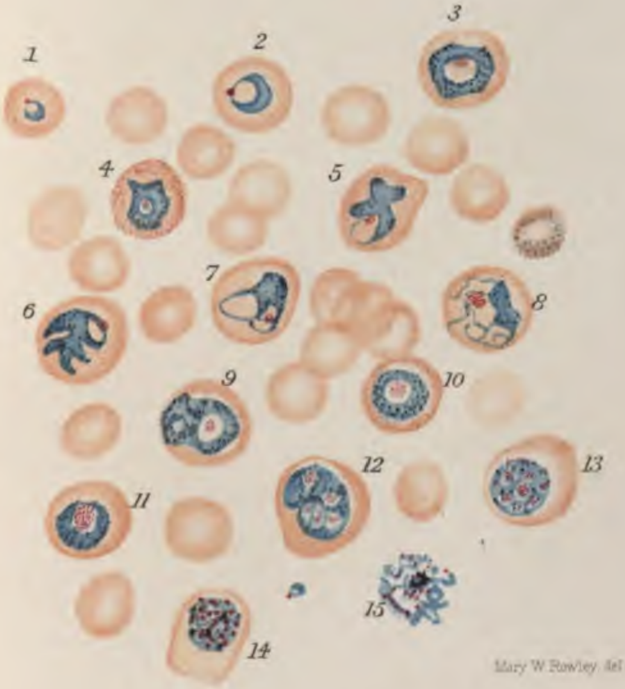
PLATE C.

The numbers correspond approximately with the stages of development. In Nos. *3* to *15* the chromatin is divided more and more and the amount of blackish pigment increases.

No. *4* shows the pink stippling often seen in infected erythrocytes; above No. *8* is a blue-stippled erythrocyte of the type seen in various anæmias.

In No. *14* (presegmenting stage) the new multiple nuclei of the future segments are seen.

No. *15*, a segmenting body, shows no sign of the red cell. One segment was fixed at some distance from the main group as if on the way to attack another red corpuscle.



Mary W Rowley, del.

THE PARASITE OF TERTIAN MALARIA.
(Wright's modification of Leishman's stain.)

Geo.H.Walker & Co. Lith.

ing out *light against the darker plasma.* This I suppose to be the remains of the corpuscle. It is not described or pictured in the standard works on the subject.

Occasionally we do find pigmented bodies wholly outside the corpuscle, either partly or fully grown. In the intracorpuscular forms the distinction between plasmodium and corpuscle substance is not, I think, so sharp and clear as one would be led to expect from the plates in standard works. With average eyes and lenses the outline of the organism, as distinguished both from its pigment granules and the surrounding corpuscle, is not easy to see.

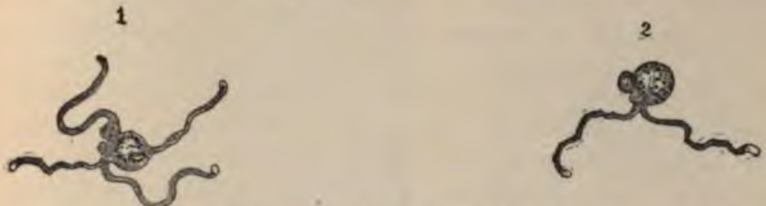


FIG. 32.—Flagellate Malarial Organisms. (After Thayer.)

But all these difficulties as well as those about recognizing the "hyaline forms" on which I expatiated in earlier editions of this book, have now been abolished for me, and should be for all students of malarial blood, by the introduction of a simple, quick, and reliable method of getting the Romanowsky stain. I refer to Leishman's stain as modified by Wright (see page 41). For diagnostic purposes I never use the fresh blood now, and I am convinced that by using the stained film specimen in every case I recognize cases of malaria that used to escape me before. For purposes of study the fresh blood is important—but not, in my opinion, for diagnosis. The method of staining is precisely that used for ordinary differential leucocyte counts and has been already described.

(*b*) *Appearance of Stained Specimens.*

For the main points the reader is referred to Plates I and C, and the descriptions accompanying them; some additional details are here added.

The youngest form of the tertian parasite seen in the red cell is identical in appearance with the *spore* of the parent rosette. It is a compact spheroidal, or slightly oval, or irregular body, about 2 μ in diameter. It shows an outer rim of basophilic protoplasm en-single large nuclear body, which is achromic to methylene stains readily in hæmatoxylon or by Nocht's method, and ch is usually enclosed or accompanied by a clear achromatic subnce, termed by Gautier "the milky zone."

In the fresh condition these bodies are noticeably refractive, e lly the nucleus, change their position but rarely their shape, are never pigmented.

The youngest tertian ring: Within a few hours after the chill parasite is usually found to have assumed a somewhat charaeistic ring shape. These bodies measure from 3–4 μ in diameter, d there is not much increase in lk for six or eight hours. The tian ring is rarely as geometrical or delicate as the æstivo-autumsignet ring. The nuclear body of the tertian ring is its most racteristic feature, appearing as a rather large, achromatic, ly refractive body, after methylene blue, but staining intensely nson with Leishman's stain.

Comparison of the Tertian and Æstivo-autumnal Rings.

I abstract here Ewing's admirable description:

1. The shape and contour of the tertian ring is usually coarse and irregular, but the æstivo-autumnal ring is geometrically circular, more delicate, with extremely fine bow, and usually with a typical signet-like swelling.

2. One or two grains of pigment are almost invariably found in the early tertian ring, but are with nearly equal constancy absent from the æstivo-autumnal signet ring.

3. The tertian ring is usually pigmented before the chromatin becomes subdivided, while the chromatin of the æstivo-autumnal ring is always subdivided before the appearance of pigment.

4. The infected cell is usually swollen from the moment of infection by the tertian spore, and commonly shrunken when harboring the æstivo-autumnal ring.

The Tertian Parasite—Later Stages.

Large tertian rings: After a period of six to eight hours the ring is usually found to have developed an outgrowth which is actively amœboid in the fresh condition and appears in stained specimens as a tongue-like protrusion or turban-shaped mass attached to one segment of the ring. The nuclear body meanwhile

Photographs by Wright & Brown, Clinico-Pathological Laboratory, Mass. General Hospital.

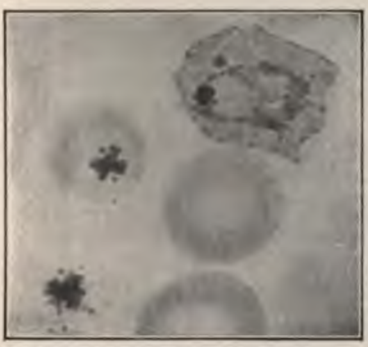


FIG. 1.—Above, on Right, a Half-grown Tertian Parasite. On left two blood-plates, one overlying a red cell.

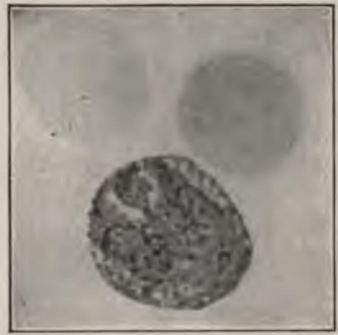


FIG. 2.—Tertian Parasite, about forty hours old. The chromatin, in the form of fine granules, is within the open space in the upper left corner of the parasite.

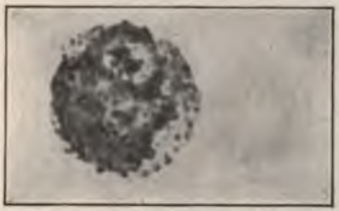


FIG. 3.—Same as Fig. 2.

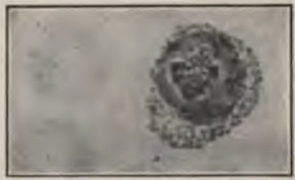


FIG. 4. — Well-developed Tertian Parasite. The chromatin appears as an irregular-shaped dark mass containing open spaces.

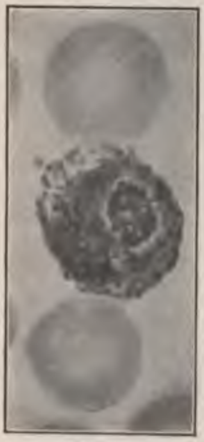


FIG. 5.—Same as Fig. 4.

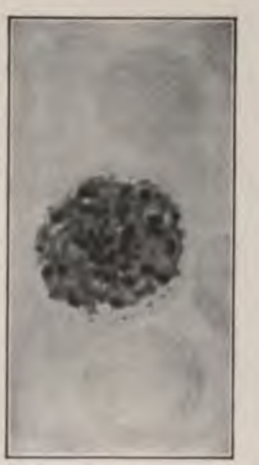


FIG. 6.—Tertian Parasite just before Segmentation. The chromatin (dark oval masses) is distributed throughout the parasite. The pigment (smaller dark points) is collected just to the left of the centre.

increases slightly in size, projecting into the ring, and the chromatin divides into several large granules.

At this period occurs the greatest amœboid activity of the parasite, and in some severe infections the organism may be found fixed in the height of its amœboid excursions. There the ring persists, but the body of the parasite is strung out into a number of slender threads with nodal thickenings.

Tertian spheroidal bodies: During the second quarter of the cycle, the body and nucleus of the parasite develop rapidly in size, amœboid motion and figures gradually diminish, and pigment is abundantly deposited in the form of dark brown or yellowish grains, showing in the fresh state active vibratory motion. The cell increases in size and its hæmoglobin diminishes. Toward the end of twenty-four hours or possibly somewhat later, the parasite occupies three-fourths of the swollen cell, in the form of a spheroidal or elliptical, homogeneous body, the outer portion of which contains most of the pigment.

Full-grown tertian parasite: The third quarter of the cycle is occupied by the continued growth of the parasite in the form of a large homogeneous, richly pigmented body, which finally occupies at least four-fifths of the swollen cell.

Presegmenting bodies usually begin to appear in the blood eight to ten hours before the chill. The pigment is gathered in a reduced number of coarse grains or spindles which lie in the body of the parasite, in a position determined by that of the new multiple nuclei (crimson stained).

Tertian rosettes are usually seen in the circulation three or four hours before the chill, most abundantly just before the chill, rapidly disappearing after the chill.

The Æstivo-autumnal Parasite.

The earliest form of the æstivo-autumnal parasite is usually to be distinguished from the tertian by the shrinkage of the cell, and by its low refractive index; it is never pigmented.

The æstivo-autumnal signet ring is a very characteristic shape assumed by the parasite at a very early period. It is noted that in some cases the rings fail to exhibit this thickening but remain of a uniform but very fine calibre throughout. Multiple infection with the young rings is very common; three parasites are often found in the same red cell, and occasionally four. The signet-ring forms frequently reach a diameter of 4 μ; beyond this size, when persisting in the peripheral blood, the growth of the parasite produces an irregular body in which the outline of the ring becomes more or less obscure. The full development of the large signet rings appears to require about twenty-four hours. In the majority of cases the ring forms seen in the peripheral blood fail to show any trace of pigment.

The later forms of the æstivo-autumnal parasite are rather rarely seen in the peripheral circulation.

The crescentic bodies: On the fourth to sixth days of any but initial paroxysms of the æstivo-autumnal infection the peripheral blood may contain red cells infected by spheroidal, oval, elliptical, or small crescentic bodies which represent the early forms of the sexual cycle of the parasite. The relation of these forms to the young amœba is not clear. A remnant of hæmoglobin surrounds the crescent. The membrane or thickened outer border of the red cell is closely applied about the convex side of the blue-stained crescent, while across the concavity it stretches loosely like a halter.

In the centre of the crescent is a sharply marked, light-blue staining or achromatic area of variable size, containing the pink-stained chromatin, and usually also the pigment.

The long persistence of crescents in the blood and their resistance to quinine are matters of common clinical observation.

The Quartan Parasite.

I have never seen a live parasite of this type. The accompanying drawings (see Plate D) are from a case of triple quartan infection, the specimen being kindly loaned me by Dr. Futcher of Baltimore. I shall attempt no description beyond that accompanying the plate.

Dr. J. H. Wright has kindly permitted the use of the accompanying photographs of the malarial parasites (see Plates V., VI., VII., VIII., and IX.).

Flagellate bodies: When blood containing crescents is allowed to stand in the air or under a cover glass for a few moments some of the crescents slowly assume the spheroidal form, active vibratory oscillations of pigment granules begin, and soon, from one or more points, pseudopodia shoot out with active lashing movements. These flagella continue their movements for some time, changing their position actively, their shape slowly, while some may be seen to break off from the body and swim off through the plasma.

ÆSTIVO-AUTUMNAL PARASITES.

PLATE VIII.

(Wright's Modification of Leischmann's Stain.)

Photographs by Wright & Brown, Clinico-Pathological
Laboratory, Mass. General Hospital.

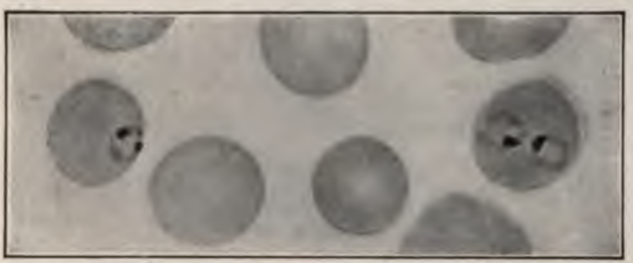


FIG. 1.—On the left a single young æstivo-autumnal parasite. On the right two within a single cell. Chromatin appears in small, dark, rounded masses.

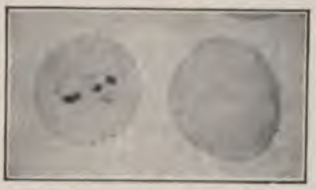


FIG. 2.—Two æstivo-autumnal parasites in one cell. In one the chromatin is divided.

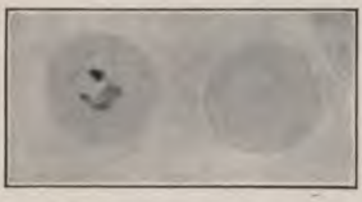


FIG. 3.—Æstivo-autumnal parasite, somewhat more developed than in the preceding figure.

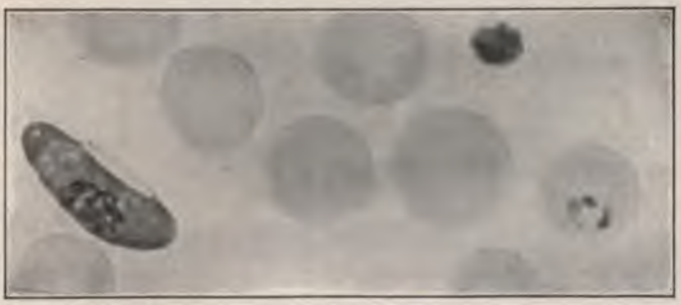


FIG. 4.—Above, a blood-plate. Below, on the right, a young æstivo-autumnal parasite. On the left a "crescent."

Tertian flagellate bodies develop from the full-grown tertian parasites in much the same way as from the crescents. Quartan parasites develop flagellate bodies very similar in appearance to those of the æstivo-autumnal type. The flagellæ are about two or three times as long as a red corpuscle and one-sixth or one-eighth as wide. Sometimes there is pigment dotted along the flagellum itself, and then we can make it out more easily. Its distal end is especially apt to be pigmented, and by the help of this pigment we make out that it is bulbous, while similar swellings can sometimes be seen at other points along the flagellum (see Fig. 33). As the pigmented end is sometimes all that we can see of it, this gives rise to the appearance of a very small, *actively locomotive* pigmented body free among the corpuscles, and its course may be followed through several fields.

When the flagella have ceased moving, their presence is generally detected, if at all, by an irregular line of pigment dots about 20 μ long, which will be shown by careful focussing to be contained within a nearly transparent membrane.

Very often we find a leucocyte in process of closing round

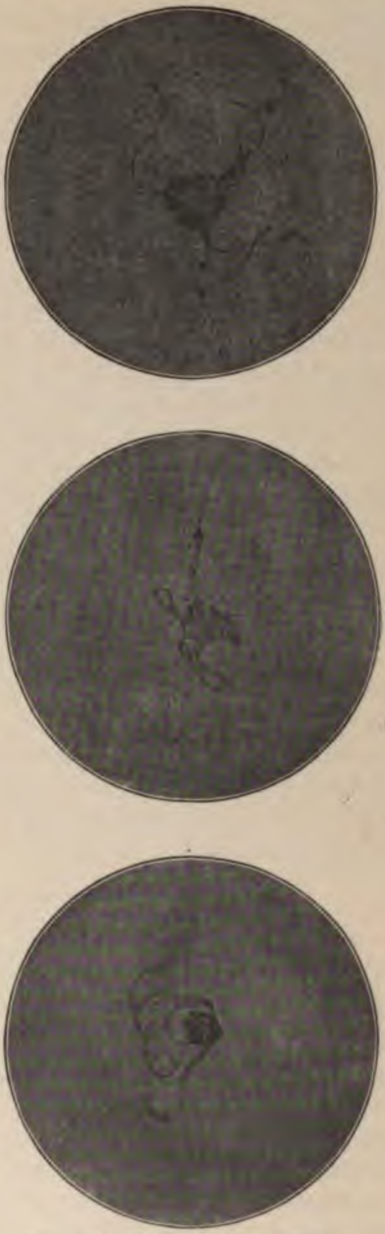


FIG. 33.—Flagellate Malarial Organisms. (After Manson's photographs.)

flagell ted parasite. Manson has lately succeeded in staining the lagellæ d the accompanying photographs are from his stained specime

I ted leucocytes, containing the whole or part of malarial organ or simply blocks or granules of black pigment, are usu- to be found in the blood near the time of the chill. The pig- be carefully distinguished from the granules present in most cytes, which in certain lights look quite dark even if un- staine rk enough to be mistaken for pigment by the untrained eye. C changing the light will easily determine wh with, provided we are familiar with the appearance ocytes in the fresh unstained blood. In certain forms of the disease in which the organisms themselves retire to the internal organs, the presence of pigmented leucocytes may be the only evidence of the disease to be found in the peripheral blood and is therefore of the greatest importance.

How long after a chill the organisms may still be found in the peripheral blood is difficult to decide, but certainly they can be found any time within twenty-four hours after the last chill, unless quinine has been given, and sometimes even if it has been given.

I have not attempted to discuss the interpretation of the different forms now believed to be sexual, or of the so-called "conjugating cycle" of the tertian parasite. I have also excluded all description of the life of malarial parasites in the mosquito and of their transmission by this insect to human beings. These tempting subjects are necessarily excluded by the plan of this book as a clinical treatise for diagnostic purposes.

OTHER CHANGES IN THE BLOOD.

Red Corpuscles.—The following is from Thayer's monograph:

"A reduction in red corpuscles follows each paroxysm; these reductions are more marked after the early paroxysms than after those occurring later. When a certain degree of anæmia has been reached the losses per paroxysm are much less. When the number of corpuscles is reduced to 2,000,000 or 1,000,000 there is little tendency toward a further fall; sometimes there may be slight rises in the curve between the paroxysms; often, however, the number of corpuscles remains stationary for weeks. In pernicious cases the number of corpuscles may fall between paroxysms." Kelsch has seen the count decrease to as small number as 583,000 per cubic

PLATE D.

Fig. 1.—The Quartan Parasite.

- *a, a, a*, etc., Youngest forms.
- *b, b* and *c, c*, Maturer forms.
- *d, d*, Presegmenting forms.
- *e*, Segmenting parasite (note the small number of segments compared with the corresponding stage of the tertian parasite).

Pigment and chromatin are more scattered than in the other forms of malarial parasite. The infected red cell is not enlarged.

Fig. 2.—The Æstivo-Autumnal Parasite.

- *1, 2, 3, 4*, Early ring forms.
- *5, 6, 8*, Maturer forms.
- *7*, Elongated form (transition to crescent?).
- *9, 11*, Crescents.
- *10, 12, 13, 14, 15*, Ovoids.

These are the only forms found in peripheral blood. Segmenting bodies occur in internal organs.

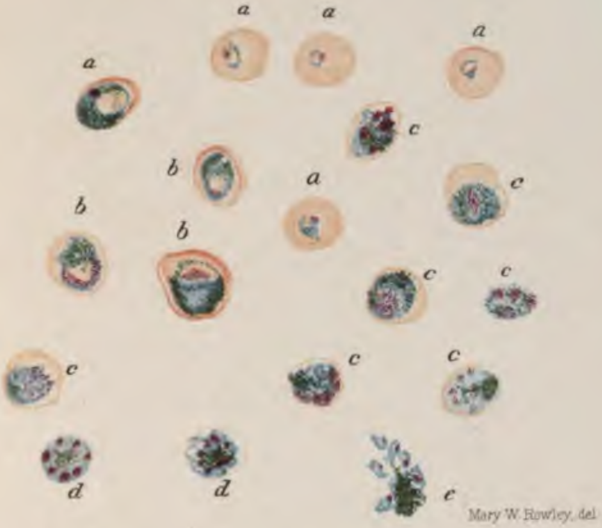


Fig. 1. THE PARASITE OF QUARTAN MALARIA.
(Wrights modification of Leishmans stain.)

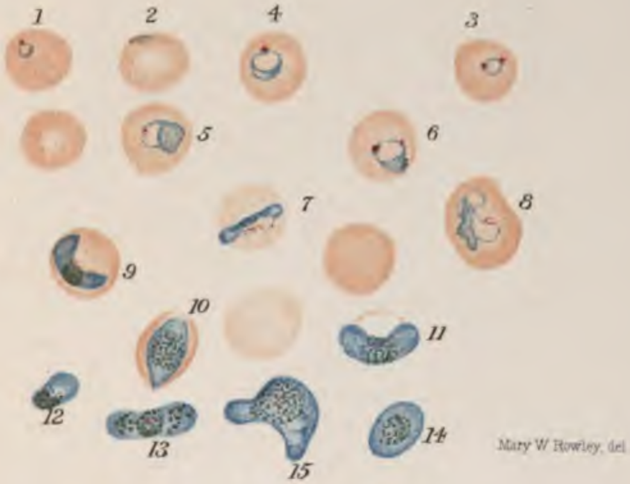


Fig. 2. THE PARASITE OF AESTIVO — AUTUMNAL MALARIA.
(Wrights modification of Leishmans stain.)

millimetre. The diminution is greater the longer the disease lasts and the more intense its manifestations are.

During the paroxysms, particularly the earlier ones, the red cells tend to *increase* in number. In tertian and quartan fevers there is a rapid and almost complete restitution of the corpuscles during the afebrile period.

In Ewing's Montauk series, there were "no less than nineteen cases in which the changes of the progressive pernicious type had been established in a period not longer than ten weeks. . . . There can be no doubt that the tendency of the æstivo-autumnal parasite is to be massed in the bone marrow. The excessive demands on red-cell production render pernicious malaria an extremely favorable condition for this disturbance of the marrow and specific megaloblastic changes."

In æstivo-autumnal fevers the number of red cells is in inverse relation to the number of young parasites, but crescentic bodies seem to have no influence on the number of red cells.

Bignami and Dionisi distinguish three types of post-malarial anæmia:

1. Ordinary secondary anæmia, with leucopenia; such cases usually end in recovery.
2. Anæmia practically identical with pernicious anæmia, megaloblasts being present, and ending fatally.
3. Anæmias which are progressive, because the bone marrow cannot compensate for the losses of corpuscles.

The rapidity of the diminution in red cells may be very great. Kelsch's count of 583,000 cells per cubic millimetre, mentioned above, was after thirty days' illness. Grawitz has seen a loss of 4,000,000 cells in six days.

Qualitative changes are those of severe secondary anæmia, anomalies of staining reaction, deformities in size and shape, normoblasts, occasional megaloblasts in the worst cases, motility in the "pale, ghostly" cells.

Hæmoglobin.—The loss of hæmoglobin bears usually a direct relation to the number of parasites in the blood. As a rule, the corpuscles and hæmoglobin are diminished proportionally (color index = 1), but sometimes the hæmoglobin is reduced disproportionately. On the other hand Delaney[1] has often found the color index *above* normal.

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[1] Delaney: Brit. Med. Jour., March 28th, 1903.

In convalescence the restitution of hæmoglobin is often incomplete; persons living in malarial districts have often a slightly smaller percentage of hæmoglobin than those living elsewhere.

The rapid diminution in the red cells is a valuable point in differential diagnosis between malaria and typhoid or pneumonia.

White Cells.—The number of leucocytes is usually subnormal, but a slight increase is shown at the beginning of the paroxysm. Following this increase there is a rapid decrease continuing throughout the paroxysm. The smallest number of leucocytes is to be seen at the end of the paroxysm when the temperature is subnormal. From this time it shows a gradual increase until the beginning of the next attack (Billings).

In a general way the white cells follow the same course as do the red.

The differential count shows a relative lymphocytosis whenever the white cells are subnormal, the larger forms of lymphocytes being especially numerous, while the polymorphonuclear cells and eosinophiles are scanty. Great stress has lately been laid by several English observers upon an increase in the percentage of large mononuclear cells (large lymphocytes) in malaria as a point of differential diagnostic value between malaria and other fevers—especially typhoid. Stephens and Christopher,[1] Türck,[2] Rogers,[3] Melland,[4] Delaney,[5] and others have substantially agreed in their findings. They state that:

1. In malaria (between paroxysms) the leucocytes are often below 2,000; in typhoid rarely so.

2. In malaria the large mononuclear forms are frequently between 12 and 30 per cent. In typhoid between 2 and 6 per cent.

3. In malaria the small lymphocytes are not increased, while in typhoid they are often 40 per cent or more.

4. In malaria myelocytes and stimulation forms are often present (1 to 5 per cent); in typhoid rarely. (These conclusions refer to and hold good for the blood of adults only.)

In the severer æstivo-autumnal paroxysms Kelsch found that the increase in the total count of leucocytes was often due to a

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[1] Stephens and Christopher: Malaria Commission of Royal Society, 5th report, 1901.

[2] Türck: *Loc. cit.*

[3] Rogers: Brit. Med. Jour., April 5th, 1902.

[4] Melland: *Ibidem*, September 27th, 1902.

[5] Delany: Brit. Med. Jour., March 28th, 1903.

(AFTER WRIGHT & BROWN.) STAINED WITH EOSIN AND METHYLENE BLUE.

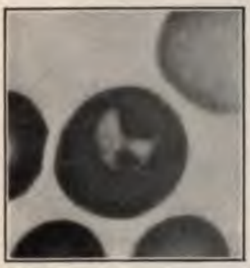

FIG. 1.—Young Non-pigmented Form (Tertian).

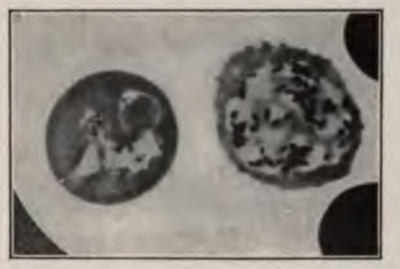

FIG. 2.—At the left, a young, pigmented tertian parasite. On the right, an adult tertian parasite. Rod-shaped pigment. The chromatin not stained.

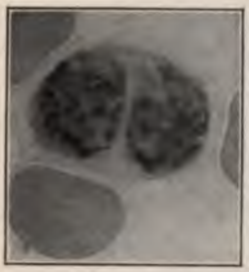

FIG. 3.—Two pigmented tertian parasites in one corpuscle.

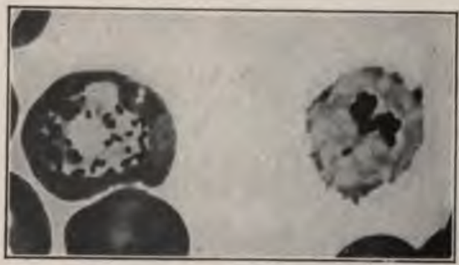

FIG. 4.—An adult tertian parasite with central vacuole and rod-shaped pigment in a distorted red blood corpuscle at the left of the figure. At the right of the figure an adult parasite with its pigment gathered together in clumps. This is a tertian parasite in the early stage of segmentation. The dark spots at the periphery of the parasite represent the remains of the red blood corpuscle which it has invaded.

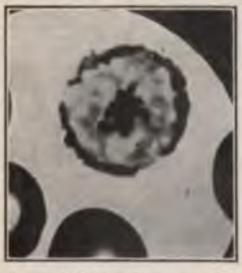

FIG. 5.—An adult tertian parasite in the same stage as the one last mentioned, with its pigment collected in a more compact manner at its central part. The irregular dark zone at its periphery is the remains of the red blood corpuscle in which the parasite has developed.

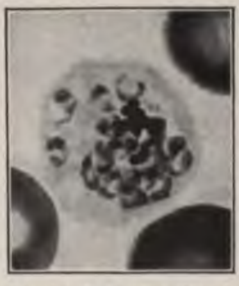

FIG. 6.—Completed segmentation of a tertian parasite. Each of the dark rounded bodies represents a young parasite. The pigment of the parasite from which they are derived is shown, as well as the faint outlines of the red blood corpuscle in which they are contained.

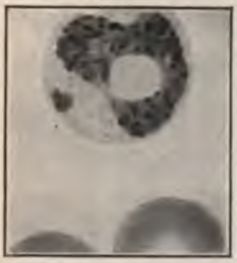

FIG. 7.—A young tertian parasite and an adult parasite with a vacuole, in one red blood corpuscle.

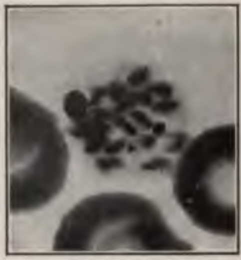

FIG. 8.—Same as Fig. 6.

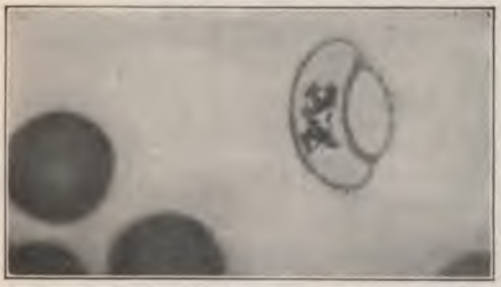

FIG. 9.—Crescentic form of the æstivo-autumnal parasite in a red blood corpuscle, which is much distorted by it. The pigment is seen in the centre of the parasite in the form of rods.

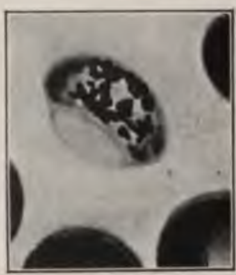

FIG. 10.—Same as Fig. 9.

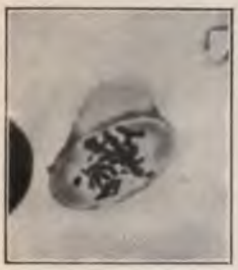

FIG. 11.—Ovoid form of the æstivo-autumnal parasite distending a red blood corpuscle. A portion of the corpuscle projects above the parasite, and is much distorted. The dark line around the parasite also represents the remnants of the corpuscle.

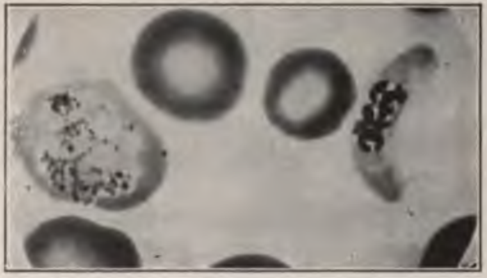

FIG. 12.—In the right of the figure is a crescentic parasite. In this photograph the blue-stained parasite is made to appear darker than the eosin-stained red blood corpuscles, by changing the character of the light used for the illumination of the specimen. The deeper staining of the poles of the parasite is shown. In the left of the figure a tertian parasite in a red blood corpuscle is shown. There was, therefore, a double infection in this case.

marked lymphocytosis; this was also observed by Ewing. The extent of the leucocytosis varies between 10,000 and 35,000 cells, the latter having been observed by Kelsch shortly before death in a comatose patient. In similar cases, often comatose, Delaney (*loc. cit.*) has seen leucocytosis of 38,000 and 14,300, and Manson records 30,000 in some "pernicious" cases.

Ziemann (*Deut. med. Woch.*, November 22d, 1900) has recently made the interesting observation that in cases of malarial infection occurring in *negroes* with spontaneous recovery, a marked leucocytosis may occur. In the summer of 1902 two cases presenting exactly these conditions came under my observation; the fever was of the tertian type with abundant and characteristic parasites, the leucocytes ranged between 19,000 and 25,000 for twenty-four hours. No other disease could be found to account for it. No quinine was given and spontaneous recovery followed.

In post-malarial anæmia Billings, Thayer, and Da Costa have found quite marked leucocytosis.

Grawitz and others have noticed an increase of eosinophiles in post-malarial anæmia. I have frequently found small percentages of myelocytes, three per cent being the highest in my experience.

MALARIAL HÆMOGLOBINÆMIA.

During the paroxysms of this form of the disease, the number of the red cells is much diminished, rouleaux are not formed, marked poikilocytosis with nucleated forms is observed. The leucocytes are increased. The regeneration is very swift, from twenty-four to forty-eight hours being usually sufficient to re-establish normal conditions.

TYPHOID FEVER AND MALARIA.

"After the first week when the typhoid fever has become fully established, active sporulation of malarial parasites is extremely rare" (Ewing).

CHAPTER XII.

DISEASES DUE TO ANIMAL PARASITES.

FILARIASIS.

ALTHOUGH most commonly found in tropical countries, one species of the filaria sanguinis hominis is not very uncommonly found in various parts of the United States. Any case of chylous urine, lymph scrotum, tumor of the groin, or elephantiasis should lead us to make a careful examination of the blood for the filaria. There are at least six species of filaria, one of which is present in the blood chiefly at night, another chiefly during the daytime, and another continuously. In Uganda and parts of India a majority of all natives carry the filariæ as "commensals" or messmates; we can hardly call them parasites since both filaria and native usually remain in good health. Only the *filaria nocturna* has thus far been seen in America (Fig. 34).

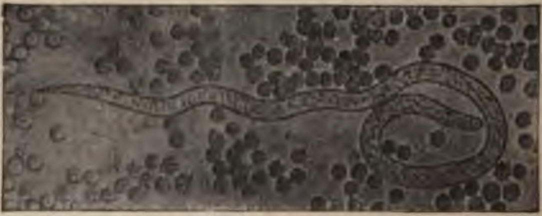

FIG. 34.—The Filaria Sanguinis Hominis. The head, curled up, is seen at the right of the cut, the tail at the left. Instantaneous photomicrograph. Four hundred diameters magnification.

In examining for the filaria a slide of the fresh blood is prepared in the usual way, *but after 8:30 o'clock in the evening,*[1] and examined at once. Lothrop and Pratt[2] counted hourly the number of embryos per cubic centimetre by drawing blood to the mark 1 in a

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[1] In persons who sleep in the daytime and work at night the habits of the filaria are said to become reversed, so that it appears in the peripheral circulation chiefly in the daytime, and is to be looked for then.

[2] Lothrop and Pratt: American Jour. of Med. Sc., November, 1900.

Thoma-Zeiss pipette, blowing it out on a cover slip and counting the number of embryos in this drop (whose size could be estimated). By this means they obtained the accompanying chart, showing the increase and decrease of filaria in the peripheral blood. One slide made at midnight contained twenty-five filariæ—the equivalent of 2,100 per cubic centimetre, or about 6,800,000 in the whole mass of the circulating blood, supposing them to have been equally distributed, as they probably are not. The embryo of this parasite (which is what we find in the human blood) is from one-ninetieth to one-seventieth of an inch in length—*i.e.*, about fifty times the diameter of a red cell, and about the width of a red corpuscle. Seen in the blood it retains its vitality and motile power for a considerable time, so that its motions may continue a week or more between slide and covers glass. Cold has little effect upon it, even freezing temperature failing to do more than make the movements slower.

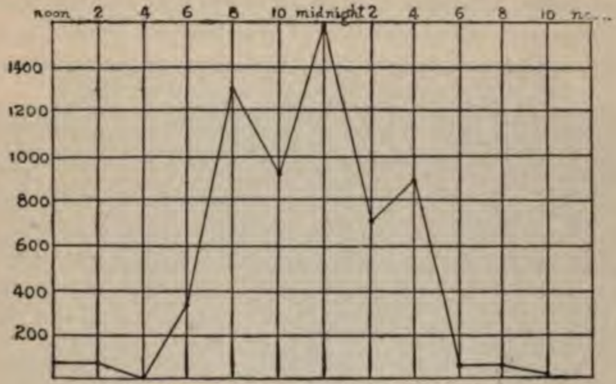

FIG. 35.—Number of Filariæ in Cutaneous Circulation.

A distinction can generally be made out between the embryo proper and its sheath (see Fig. 36). From this sheath the embryo escapes when in the blood of the mosquito, which insect acts not infrequently as intermediary host and conveys the parasite indirectly from man to man through the medium of water. After sucking in the organism with the blood the mosquito lays its eggs and dies in some neighboring pond or stream whence the filaria again gains access to men.

It is a long, slender, snake-like, gracefully shaped worm, and when alive its activity is so great that measurements and observations of its structure cannot be made till it is paralyzed by approaching death (Fig. 37).

Posteriorly it tapers for one-fifth its length down to a very sharp point. The extreme end of the tail often looks as if articulated, for it does not harmonize with the general curve of the body, but lies bent at an angle. Toward the head it tapers very slightly, and when alive a "pouting" movement as if of breathing can be seen at its very extremity. About the middle of the body a granular aggregation can be made out along the central axis of the animal. Except for this granular portion the parasite is so translucent that it is not easy to make it out at first. The distinction of body and sheath mentioned above appears as a "clear space" at each end of the body (*vide* Fig. 36). After the motions have ceased it becomes darker and traces of transverse striation may be seen (Fig. 38).

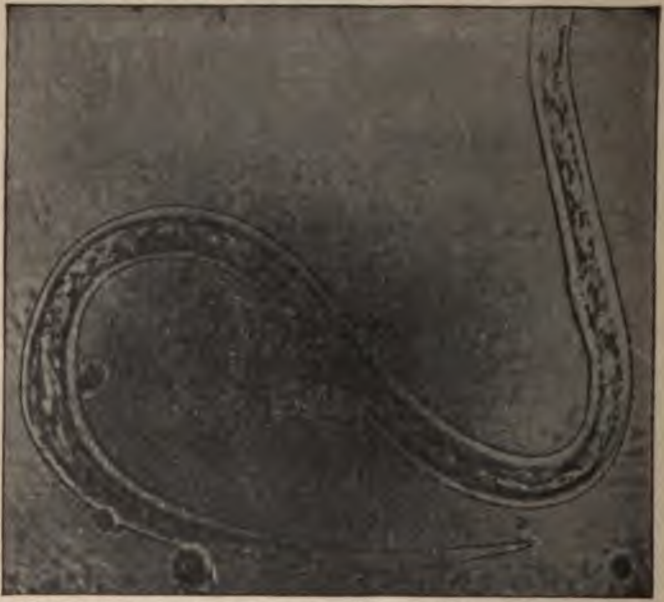

FIG. 36.—Tail of Filaria, showing Prolongation of the Sheath beyond the End of the Embryo Itself. Magnified 800 diameters.

It has no locomotive power and confines itself to wriggling in the same spot. Saussure[1] says he has watched them "fighting with each other for hours."

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[1] Philadelphia Medical News, June 28th, 1890, where he reports twenty cases seen in Charleston, S. C.

The head of the filaria is said by some authorities to be supplied with feelers or flagella, and Manson describes what he calls a "cephalic armature" or fang (Fig. 39).

The same organism can sometimes be found in the chylous urine, but not every case of chyluria is due to the filaria sanguinis hominis. In a considerable portion of cases no such organism is to be found.

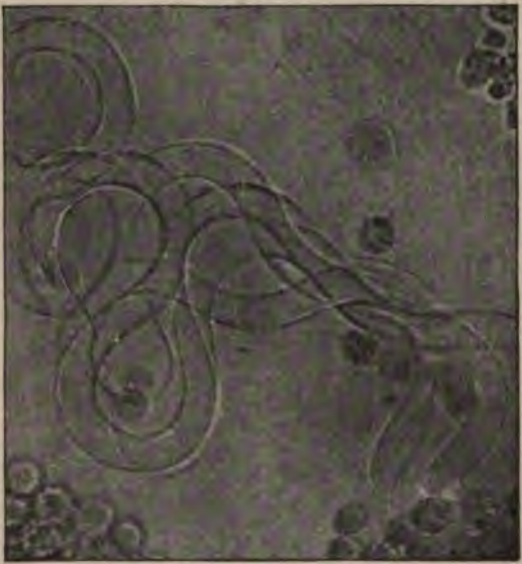

FIG. 37.—The Movement of a Single Filaria during Four Successive Exposures of One-fifth of a Second Each, the Entire Series Occupying less than Five Seconds. Magnified 800 diameters.

Henry[1] succeeded in staining the parasites *intra vitam* by giving the patient considerable doses of methylene blue internally for some weeks. Only a faint bluish tinge was imparted, however, to the organism by this method.

For finding the parasite it is best to use a low power, not an immersion lens, and the whole of several slides should be looked over.

Specimens can be dried and preserved for staining provided we do not heat them over a lamp or pass them through a flame. Fixation in alcohol and ether and staining with thionin work well. Manson[2] stains with eosin and mounts in "glycerin jelly."

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[1] Med. News, May 2d, 1896.

[2] "The Filaria Sanguinis Hominis," by Patrick Manson, M.D., Amoy, China, 1883.

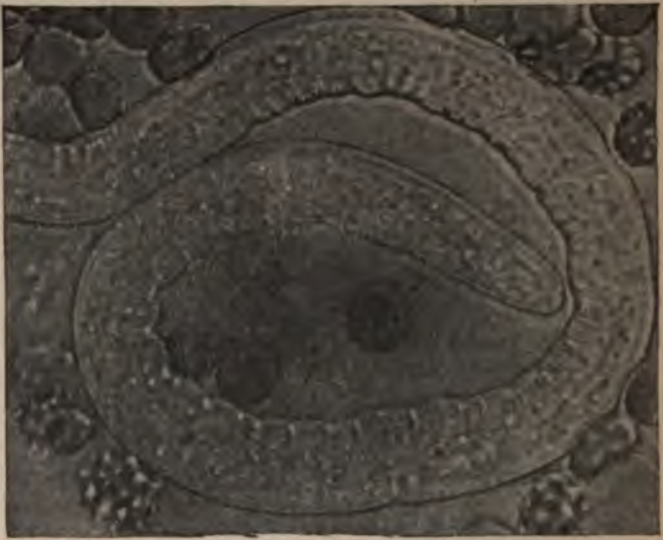

FIG. 38.—Head of Filaria. Shows structure and beginning granular degeneration. Magnified 1,500 diameters.

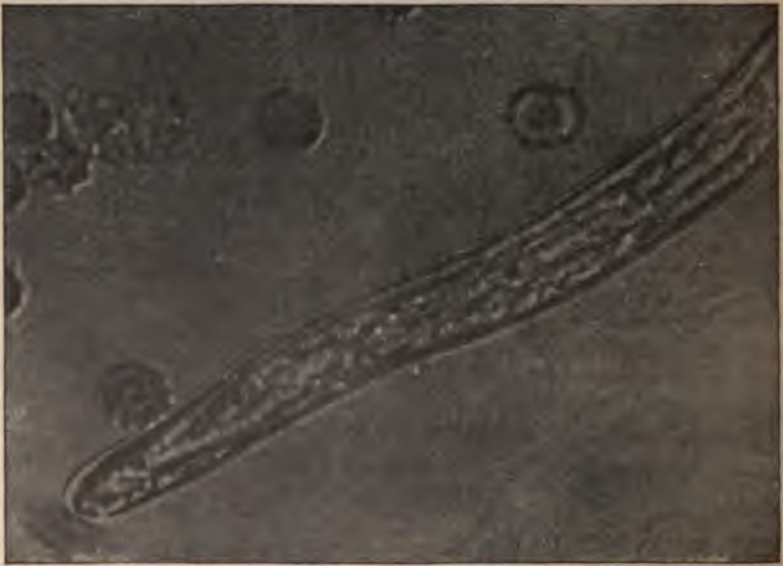

FIG. 39.—Head of Filaria Magnified 1,500 Diameters. The blur in front of the head may be due to the motion of flagella.

Several other species have been observed in England in negroes from the Congo River, but not hitherto in America.

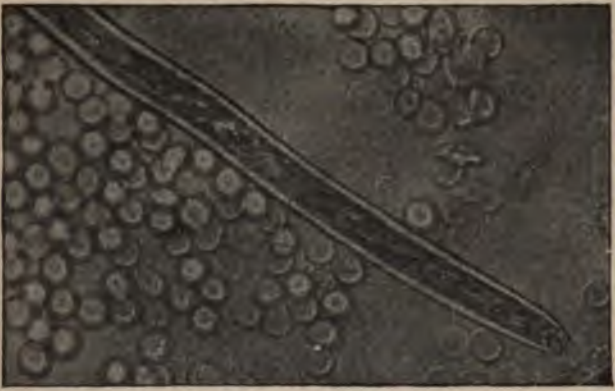

FIG. 40.—Head of Filaria Overlapping a Red Corpuscle. The appearance might be mistaken for the cephalic end of a sheath.

Considerable interest has lately been aroused in the morphology of the blood in filariasis:

Case.	Red cells.	White cells.	Per cent hæmoglobin.	Per cent polynuclears.	Per cent lymphocytes.	Per cent large mononuclear.	Per cent eosinophiles.	Remarks.
1	4,876,000	....	88	63.9	23.1	9	3.4	Da Costa.
2	4,200,000	8,000	88	55.7	34.2	.6	9.5	Da Costa.
3	....	6,500	93	56.6	35.3	3.6	4.3	Da Costa.
4	6,016,000	8,000	93	55.8	38.2	1.4	4.6	Lothrop and Pratt.
5	....	....	..	34	44	7	15	Coles.[1]
6	....	....	..	43	33.8	6.5	17	Coles.
7	....	6,800	..	68.5	24.5	*	7	December 1st. 4 P.M.
		1,250	..	55.5	32.5	*	12	December 11th, 11 P.M.
		4,600	..	57.5	36.5	*	6	December 12th, 10 A.M.
		13,100	..	59	31.5	*	9.5	December 12th, 11 P.M.
		5,000	..	65	32	*	3	January 31st, 10 A.M.
		6,300	..	66	29	*	4.5	January 31st, 3 P.M.
		10,100	..	61	31	*	8	January 31st, 10 P.M.
		10,600	..	67	26	*	7	February 8th, 10 P.M. Gulland.[2]
8	....	....	..	52.5	40.5	*	7	Gulland.[2]
9	....	....	..	....	....	....	7.5	Vaquez.[3]
10	....	....	..	....	....	....	12	Sicard.[4]

* Included with lymphocytes.

[1] Coles: Brit. Med. Jour., May 10th, 1902.

[2] Gulland: Brit. Med. Jour., April 5th, 1902.

[3] Vaquez: La Sem. Méd., December 17th, 1902.

[4] Sicard: *Ibidem.*

In the preceding table I have arranged some of the briefer records. The best studied cases are those of Calvert[1] which are exhibited in the following table.

TABLE CIX.—CALVERT. CASE I.

Date.	Hour.	White cells.	Polynuclears, per cent.	Lymphocytes, per cent.	Large mononuclears, per cent.	Transitionals, per cent.	Eosinophiles, per cent.	Filariæ.	Red cells.
April 18th................	9 A.M.	23,000	60	12	4	4	20	0	4,720,000
	10 A.M.	18,000	65	12	4	2	17	0	
	11 A.M.	18,600	65	9	3	3	20	0	
	12 M.	18,500	59	11	6	3	21	0	
	1 P.M.	26,600	60	10	4.5	2.5	20	0	
	2 P.M.	24,400	58	10	5	5	22	0	
	3 P.M.	20,000	60	11	4	4	21	0	
	4 P.M.	18,600	67	12	3	3	15	0	
	5 P.M.	18,000	65	11	5	3	16	0	
	6 P.M.	20,000	63	14	5	5	13	84	
	7 P.M.	......	61	16	5	5	12.5	252	
	8 P.M.	......	60	14	4	3	19	504	
	9 P.M.	......	68	13	5	3	11	672	
	10 P.M.	......	65	13	5	2	15	840	
	11 P.M.	......	65	15	4	3	15	1,176	
	12 M.	......	67	12	5	3	8	840	
April 19th................	1 A.M.	......	65	12	4	2	17	672	
	2 A.M.	......	64	10	3	2	21	840	
	3 A.M.	......	69	10	3	3	15	672	
	4 A.M.	......	71	11	3	3	11.5	672	
	5 A.M.	......	64	11	4	3	18	504	
	6 A.M.	......	65	12	4	3	15	504	
	7 A.M.	18,600	63	13	3	3	17.5	84	
	8 A.M.	22,000	65	13	4	4	14	0	
	9 A.M.	18,600	64	12	4	3	16	84	
April 27th................	9 A.M.	23,000	68	13	3	2	....	84	5,200,000
May 1st................	10 A.M.	18,000	60	16	4	2	18	252	5,200,000
May 6th................	2 A.M.	20,000	66	12	4	3	15	0	5,160,000
May 8th................	8 A.M.	17,000	66	13	4	3	14	0	5,200,000

TABLE CX.—CALVERT. CASE II.

Date.	Hour.	Red cells.	White cells.	Polynuclears, per cent.	Lymphocytes, per cent.	Large mononuclears, per cent.	Transitionals, per cent.	Eosinophiles, per cent.	Filariæ.
April 18th..............	......	3,600,000	8,000	64	14	4.5	2.5	15	
April 23d..............	2 P.M.	3,550,000	7,600	68	19	3.5	3	6.5	84
	3 P.M.	....	8,000	70.5	15	3.5	3	8	0
	4 P.M.	....	8,000	66	19.5	4.5	2	8	0
	5 P.M.	....	6,600	67	20	3	2.5	7.5	84
	6 P.M.	....	13,000	66	20	4	3	7	84
	7 P.M.	....	......	68	20	3	2	7	504
	8 P.M.	....	......	70	16	4	3	6.5	588
	9 P.M.	....	......	64.5	23	3	3	6.5	1,680
	10 P.M.	....	......	67	18	4	4	7	1,596
	11 P.M.	....	......	64.5	22	4	2.5	7	1,512
	12 M.	....	......	65	21	3	2	6	1,428

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[1] Calvert: Johns Hopkins Bull., June, 1902.

TABLE CX.—CALVERT. CASE II. (*Continued*)

Date.	Hour.	Red cells.	White cells.	Polynuclears, per cent.	Lymphocytes, per cent.	Large mononuclears, per cent.	Transitionals, per cent.	Eosinophiles, per cent.	Filariæ.
April 24th	1 A.M.	....	......	65	22	3	2	8	1,008
	2 A.M.	....	......	65	22	3	3	3	1,008
	3 A.M.	....	......	67.5	22	3	1.5	6	840
	4 A.M.	....	......	67.5	19	3.5	2	8	612
	5 A.M.	....	......	61	18.5	4	2	14.5	504
	6 A.M.	....	8,600	64.5	19	3	3	10.5	168
	7 A.M.	....	12,000	60.5	32	3	2	12.5	756
	8 A.M.	....	10,600	60	25	4	3	8	1,092
	9 A.M.	....	8,600	60.5	15	2.5	1.5	20.5	336
	10 A.M.	....	7,000	65	11	4.5	2	12.5	588
	11 A.M.	....	7,600	64	16	4	2	15	336
	12 M.	....	8,000	66	15	4	2	15	84
	1 P.M.	....	10,000	68	14	4	2	12	0
	2 P.M.	....	8,000	64	20	4	2	11	84
May 6th	......	3,289,000	14,000	52	26	6	3	13	336
May 8th	2 P.M.	3,500,000	12,000	60	20	6	2	12	0

From these cases it appears that eosinophilia is a constant feature of recently acquired cases and occurs to a less extent in chronic cases. It is usually most marked in the hours when filariæ are fewest in the peripheral blood and decreases as the filariæ increase.

SPIROCHÆTE OF RELAPSING FEVER.

During the febrile paroxysms of relapsing fever, and for one or two days before them, Obermeyer and others have found constantly present in the peripheral circulation a parasite whose length averages about six times the diameter of a red corpuscle. Even under high-power lenses it is a mere thread in width, curled upon itself like a corkscrew and actively motile, so that in examining the blood with a low power we get a "peculiar impression of disturbance" among the red cells.

The number of twists in this spiral-shaped organism varies a good deal, and one of its motions consists in contracting and extending itself like a spiral spring. It can thus multiply its own length three or four times. It has also a delicate, wavy, but rapid motion along its long axis. The whole thread, or a part of it only, may have these motions. Further, the whole parasite has power of locomotion apparently independent of the currents in the blood plasma of a slide and cover-glass specimen. Its locomotion is slow compared to the movements above described. Particularly in the blood post mortem they are apt to wind themselves into each other so as to seem much larger than they actually are, and sometimes a large "nest" of them may look like a leucocyte, except for the fine wavy threads which can be seen in motion at the periphery of the mass.

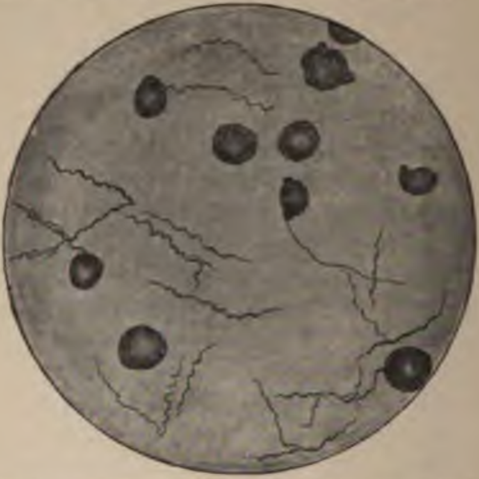

FIG. 41.—Spirochætes of Relapsing Fever in Human Blood.

The number present in the blood is very much smaller at the beginning of a paroxysm than after the second day. During the first few hours of a febrile period Mocyntkowsky could find only one spirochæte in ten or twenty microscopic fields, while later on he

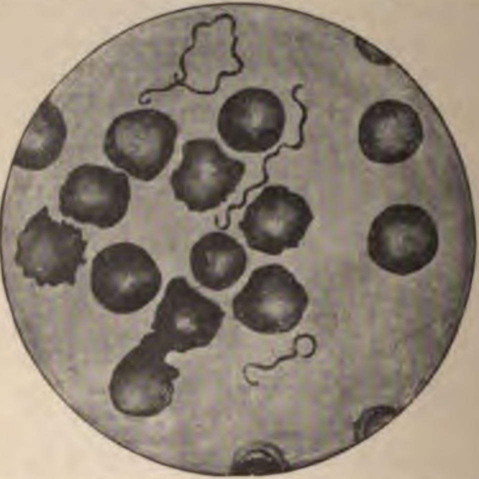

FIG. 42.—Spirochætes of Relapsing Fever in Human Blood.

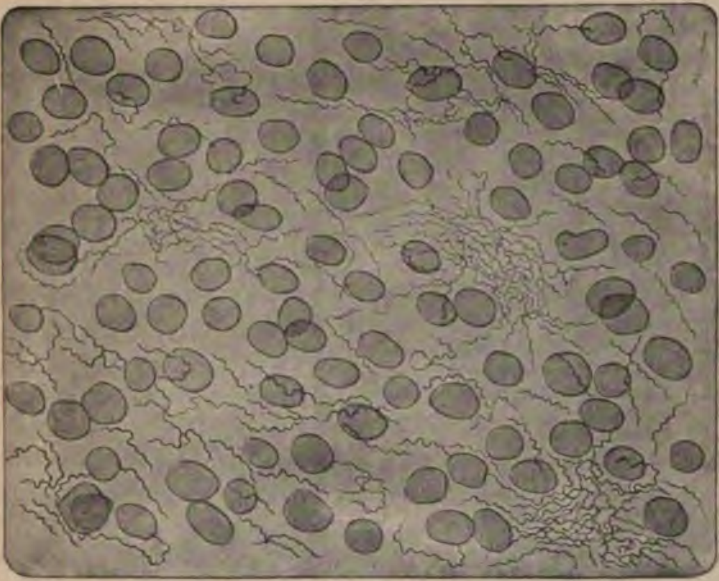

FIG. 43.

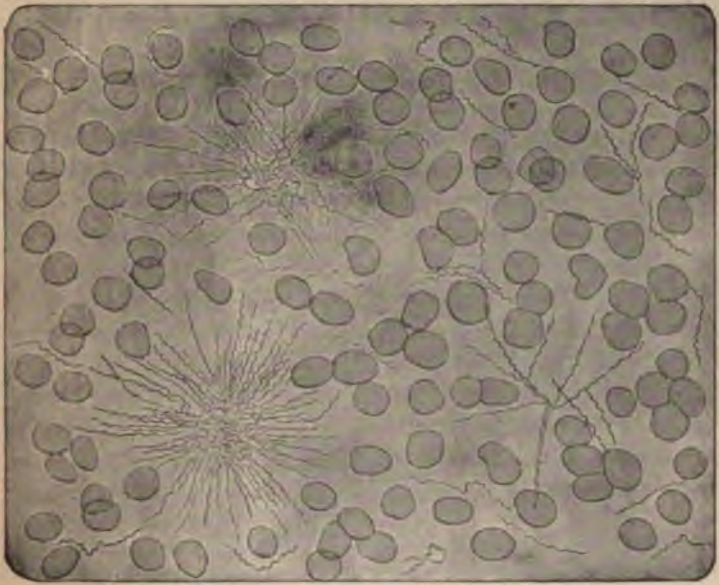

FIG. 44.—Spirochætes of Relapsing Fever.

saw twenty or thirty of them in a single field. There are usually more parasites with each successive paroxysm.

Blood taken from different parts of the body often shows a great difference in the number of organisms to be found. The life history of a single parasite seems to be very short, but they multiply with the greatest rapidity. Albrecht has seen them so increase within six hours that whereas at first he saw only a few in the whole slide he later found many in each field. As the spirochæte dies, its movements get languid, and finally it breaks up into small granular bits (spores?).

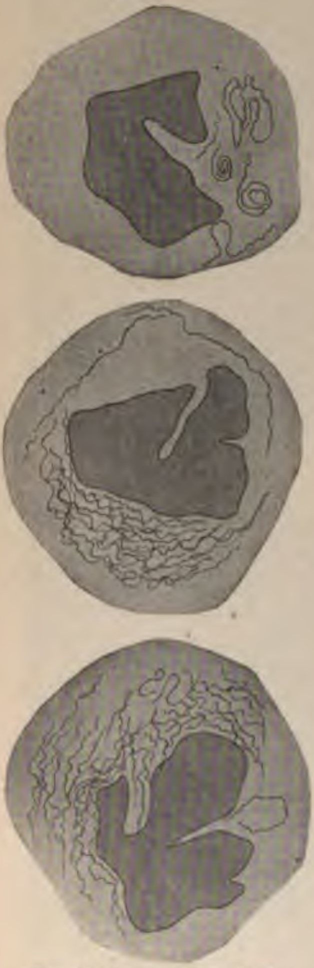

FIG. 45.—Leucocytes Containing Spirochætes.

Between paroxysms the spirochætes are not found, but there are to be seen peculiar highly refractile globules compared by v. Jaksch to a diplococcus. The latter author believes that he has seen these develop into the spirochæte at the beginning of a paroxysm and hence believes them to be spores.

This spirochæte is found in all cases of relapsing fever and in no other known disease, so that like the plasmodium malariæ it is pathognomonic and of the highest importance.

Anæmia and leucocytosis (during the paroxysm) are among the secondary results of the presence of this parasite in the blood.

Boeckman reported that the red cells sink during, and for one to two days after, the attack, increasing somewhat in the afebrile periods.

Laptschinsky, Heidenreich, and Boeckmann all noted considerable leucocytosis. Laptschinsky mentioned the presence of a very large number of coarsely granular leucocytes.

A certain resemblance has been noted between the spirochæte and a free flagellum broken off from a malarial parasite, but the clinical history and the presence or absence of other evidence of malaria in the blood would easily decide the question of diagnosis.

Technique of Examination.—As in looking for the malarial organism, it is best to examine the blood fresh between a slide and cover-glass (*vide* page 7) and to use an oil-immersion lens. In dried specimens the organism can be stained with fuchsin, but it is much more difficult to recognize than in the fresh blood. The spirilla stain well with aniline dyes, and Karlinski succeeded in demonstrating flagella with some individuals. Concentrated solution of methylene blue stains all spirilla in from two to five minutes. Phagocytosis (see Fig. 45) can easily be watched in the peripheral blood.

SPOTTED FEVER (TICK FEVER) OF THE ROCKY MOUNTAINS.

The parasite of this newly described disease was first discovered by Drs. L. B. Wilson and W. M. Chowning[1] of the University of Minnesota, whose services were engaged in the spring of 1902, by the Montana State Board of Health, to investigate an epidemic then prevailing in the Bitter Root Valley. Their report was published July 19th, 1902. Their findings were confirmed by Surgeon J. O. Cobb,[2] by Prof. F. F. Wesbrook,[3] of the University of Minnesota, and by Passed Assistant Surgeon John F. Anderson[4] of the United States Hygienic Laboratory at Washington. Altogether seventeen cases have been examined with positive findings in all. The parasite most resembles that of Texas cattle fever as described by Theobald Smith (*pyrosoma bigemium*).

It is found chiefly in the red cells but occasionally outside; is non-pigmented and shows amœboid movements. Three forms are described: "The most common is a single ovoid body, highly refractile and usually situated near the edge of the cell." While the slide is warm the parasite projects pseudopodia rapidly and slightly changes its position. It is 1.5 to 2 μ long and half as wide and resembles the youngest parasite of æstivo-autumnal malaria. "Another form, less common, is larger, especially at one end where a dark granular spot appears." A third form, distinctly pyriform, is arranged in pairs, with the smaller ends approaching and sometimes joined by a minute thread. In this no motion is seen.

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[1] Wilson and Chowning: Report of Montana Board of Health, 1901–02; Journ. American Med. Assn., July 19th, 1902.

[2] Cobb: Public Health Reports, August 15th, 1902.

[3] Wesbrook: Report of Minnesota Board of Health, 1901–02.

[4] Anderson: Hygienic Laboratory, Bulletin No. 14, July, 1903 (Washington, D. C.).

The parasite is best stained by some method giving the Romanowsky stain. It stains blue against the pink of the red corpuscles, but it is always difficult to bring it out clearly. The parasite takes the stain more deeply at one end. Sometimes it has a central stained spot surrounded by a clear unstained space.

In specimens stained by some one of the Romanowsky stains (Nocht's, Jenner's, Wright's) the parasite sometimes shows a red or violet chromatin body, while the rest of the body stains blue against the pink of the corpuscles. It is usually necessary to search several fields before finding a parasite, but rarely as many as eleven occur on a single field. Aside from the presence of these parasites the blood shows only an anæmia. Throughout the course of the disease there is "a steady but never very rapid decrease in the percentage of hæmoglobin, one case going as low as fifty per cent." The erythrocytes are sometimes moderately diminished. The leucocytes are not increased or diminished. In the two differential counts on record thus far a slight increase in the large mononuclear forms was noticed.

DISTOMUM HÆMATOBIUM (BILHARZIA DISEASE).

Eosinophilia has recently been reported. The following figures exemplify it:

Red cells.	White cells.	Per cent hæmoglobin.	Per cent polynuclears.	Per cent. small lymphocytes.	Per cent large mononuclears.	Per cent eosinophiles.	Reported by
4,650,000	8,200	84	49	21	18	12	Manson.[1]
			46	27	7	20	Coles.[2]

Douglas and Hardy (*Lancet,* October 10th, 1903) studied 50 cases, and found leucocytosis and an eosinophilia averaging 16.5 per cent; 21 cases showed over 15 per cent of eosinophiles, and but 2 were below 6 per cent. Despite the absence of malaria the large mononuclears averaged 12.5 per cent, 10 being above 15 per cent.

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[1] Manson: Brit. Med. Jour., December 20th, 1902.

[2] Coles: *Ibidem,* May 10th, 1902.

FRAMBŒSIA.

Glogner[1] in eight cases found an increase of lymphocytes, slight or marked.

TRYPANOSOMIASIS.

The first discovery of a trypanosoma in human blood was made in Gambia, in 1901, by Dutton,[2] of Liverpool, who found it in two persons, one a child without symptoms, the other an adult Englishman with chronic fever, wasting, splenic enlargement, and circumscribed, fugitive œdema. Laveran, referring to these cases, dubs the parasite Trypanosoma Gambiensis,[3] and states that it is conveyed to man as to other animals by the fly Glossina palpalis.

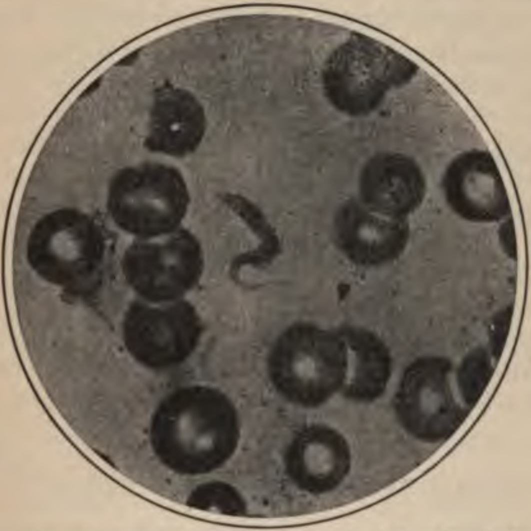

FIG. 46.—Trypanosoma in Human Blood. (By permission of Dr. J. Everett Dutton and the London *Lancet*.)

An expedition sent to Gambia in 1902 by the Liverpool School of Tropical Medicine[4] found 5 cases among 221 examined; the number of parasites was from 1 to 23 per cover slip (see Fig. 46).

These observations have been confirmed by Forde,[5] Daniels,[6]

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[1] Glogner: Virchow's Arch., vol. 168.

[2] Dutton: Brit. Med. Jour., September 20th, 1902.

[3] Laveran: Bull. de l'Acad. de Méd., May 27th, 1902.

[4] Referred to in Brit. Med. Jour., February 7th, 1903.

[5] Forde: Jour. of Tropical Med., September, 1902.

[6] Daniels: *Ibidem*, November, 1902.

Maxwell Adams,[1] Manson,[2] Leishman,[3] Baker[4] (three cases), and others. Some anæmia results in chronic cases. About twelve cases in all are now on record.

Manson[5] describes the human trypanosome as seen in the fresh blood as "a minute, colorless, transparent and very active vermicule tapering toward its extremities, one of which ends in a long flagellum continuous with the undulating membrane attached to nearly the entire length of one side of the body." Near the end opposite that bearing the flagellum is "a refringent speck—the centrosome. The organism is always free in the plasma, never intracorpuscular."

Stained by any of the Romanowsky stains (*e.g.*, Wright's) the body of the parasite is blue, the flagellum and the free edge of the undulating membrane are pink, the centrosome is deep red, while a nucleus, also pink staining, appears about the centre of the body.

The length of the parasite is from two to three times that of a red cell; its width about one-fourth of that of a red cell. When in activity it rotates with a screw-like motion upon its long axis. The number of parasites found in the cases thus far observed has been scanty—three to eight in a three-fourth inch cover-slip preparation.

This trypanosome has also been found by Castellani, Bruce, and others, in the blood and cerebro-spinal fluid of cases of sleeping-sickness, and is believed by Manson to be the cause of this disease.

ANÆMIA DUE TO INTESTINAL PARASITES.

The bothriocephalus latus, uncinaria duodenale, and a few other parasites are capable of producing by their presence in the intestine a very severe anæmia, which may be indistinguishable from pernicious anæmia. Bothriocephalus anæmia has been studied by Schaumann in a monograph (Berlin, 1894, Hirschwald) which is the very acme of careful, conscientious work and eclipses entirely the fragmentary observations of earlier writers. Uncinariasis has been thoroughly studied by B. K. Ashford of the United States army in Porto Rico, by Boycott and Haldane,[6] Sandwith, and others.[7]

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[1] Maxwell and Adams. Brit. Med. Jour., March 28th, 1903.

[2] Manson: Brit. Med. Jour., May 30th, 1903.

[3] Leishman: Brit. Med. Jour., May 30th, 1903.

[4] Baker: *Ibidem.*

[5] Manson: "Tropical Diseases," 1903.

[6] Boycott and Haldane: Journ. of Hygiene, Jan., 1903.

[7] See p. 490.

BOTHRIOCEPHALUS ANÆMIA.

The presence of the bothriocephalus latus in the intestine of man is usually accompanied by anæmia. In certain cases, however, under conditions not at all clear at present, there is produced an anæmia of the severest type, differing from ordinary pernicious anæmia only in its curability through the expulsion of the worm.

Schaumann's magnificent study of the blood of thirty-eight cases resulted in the following data:

1. *Red cells* at time of first examination:

2,000,000 to 2,500,000 in 1 case (2,150,000).
1,500,000 " 2,000,000 " 9 cases.
1,000,000 " 1,500,000 " 17 "
500,000 " 1,000,000 " 10 "
Under 500,000 " 1 case (395,000).
38 cases
Average of all, 1,290,000.

2. *Hæmoglobin* (first test):

30 to 40 per cent in 7 cases.
20 " 30 " " 18 "
10 " 20 " " 13 "
38 cases
Average, 25 per cent.

3. *Color index:* Less than 1 in 8 cases (0.9 to 0.99), more than 1 in 30 cases. Average, 1.09.

4. Average diameter of red cells, 7.4 μ (slightly above normal).

5. Poikilocytosis marked, but its degree is not parallel with the degree of anæmia.

6. Rouleaux formation always defective or altogether absent.

7. Polychromatophilia and stippled red cells are common.

8. *Nucleated red cells* present in all cases examined for them—26—but without parallelism with the degree of anæmia.

Megaloblasts predominated in over half the cases. In 5 cases megaloblasts *only* appeared; in one case normoblasts only. In the other 20 cases both types were present. Mitoses were found in 2 cases.

Leucocytes were usually normal or subnormal in number.

Differential count practically as in pernicious anæmia.

The eosinophiles are noted as "very scanty" in 25 cases and "apparently somewhat increased" in one case. [This is in sharp contrast with the eosinophilia usually present in ankylostomiasis (*vide* page 116.)] A few myelocytes were noted in two cases with leucocytosis

Blood plates diminished.

So far the figures refer to untreated cases at the worst stage of the disease. Five-sixths of the cases were entirely and apparently permanently cured in about two months by the expulsion of the worms. Blood counts at the time of leaving the hospital showed:

In 3 cases about 2,500,000 red cells
" 2 " " 3,000,000 " "
" 2 " " 3,500,000 " "
" 16 " " 4,000,000 " "
" 4 " " 4,500,000 " "
" 4 " " 5,000,000 " "
Average 4,680,000 (16 cases still higher) with 70 per cent hæmoglobin.

Thirteen of these were followed up after discharge, and in these a full *restitutio ad integrum* occurred.

UNCINARIASIS (ANKYLOSTOMIASIS).

The first careful observations of the blood of which I have knowledge are those of Zappert in 1892,[1] who reported a moderate grade of anæmia with low color index.

Müller and Rieder[2] were the first to note the eosinophilia which later observations have shown to be so frequent. They record 8.2 per cent and 9.7 per cent in two cases of the disease Zappert refers to two cases with 17 per cent of eosinophiles.

Rogers[3] compares the anæmia produced by the uncinaria with that due to malaria and with the blood of the average native of Assam, where his studies were carried on His results are shown in the following table:

	Red cells.	White cells.	Hæmoglobin.
Healthy Assamese	4,734,000	7,325	67 per cent.
Chronic malaria	2,000,000	1,600	31 "
Ankylostomiasis	1,145,000	5,338	15 "

Rogers does not refer to the percentage of eosinophiles.

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[1] Zappert: Wien. klin. Woch., 1892, No. 24.

[2] Müller und Rieder: Arch. f. klin. Med., vol. xlviii.

[3] Brit. Med. Journal, 1900, p. 589.

In 1894 Bucklers[1] reported the following counts:

	Case I.	II.	III.	IV.	V.	VI.
Red cells	3,649,000	......	3,954,000			
White cells	13,000	15,000	20,600			
Hæmoglobin	......	......	45.0%	....	21%	25.0%
Eosinophiles	16%	4%	53.6	10.4%	22	21.2
Polynuclear	46	74	22.3	46	53	32.2
Lymphocytes and transitionals	37	22	25.1	43.6	25	46.6

Leichtenstern (referred to by Ehrlich and Lazarus) illustrated the behavior of the eosinophiles in the presence of a secondary infection by this case: "In the blood of a very anæmic, almost moribund patient with ankylostomiasis there were found, in 1897, 72 per cent of eosinophiles. The patient contracted a croupous pneumonia, and in the high febrile period of the disease the eosinophiles sank to 6 and 7 per cent, rising again after the termination of the pneumonia to 54 per cent. After removal of the worms the eosinophiles fell at once to 11 per cent.

"In 1898, when the fæces contained but very few ankylostomata, . . the eosinophiles amounted to 8 per cent."

The Blood in Gross

The best studies of the disease are those of Ashford[2] and of Boycott and Haldane.[3] The latter studied an epidemic observed in Cornwall miners. They found the total volume of blood (Haldane's method—see above, page 6) increased as in chlorosis and very different in this respect from the conditions found in pernicious anæmia. Indeed they insist that the blood of uncinariasis rarely simulates to any extent that of pernicious anæmia.

Red Cells and Hæmoglobin

Their counts varied from 1,500,000 to 5,400,000 in 33 cases. The color index was *low* in all but 4 cases,—the lowest figures being 0.53 and the highest 1.38 (17 per cent to 104 per cent). In general the more profound the anæmia, the less the tendency to a high color index such as is the rule in pernicious anæmia.

In most of their cases the loss of red cells was not extreme;

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[1] Bucklers: Münch. med. Woch., 1894, No. 2.

[2] Ashford: Amer. Med., 1903, p. 391.

[3] Boycott and Haldane: Jour. of Hygiene, 1903, vol. iii., No. 1.

poikilocytosis was present in but few cases and never extreme; a few showed variations in size beyond the normal. In one case (with 1,500,000 red cells) the cells showed polychromasia with five normoblasts, two questionable megaloblasts, and abundant megalocytes; two other cases showed one or two normoblasts.

This epidemic was a comparatively mild one, which probably accounts for the difference between these blood changes and those reports by Ashford, among which 16 out of 50 showed less than 2,000,000 red cells per cubic millimetre. Of a former series of 19 cases,[1] 11 fell below 1,000,000, 14 had normoblasts, and 6 of them showed megaloblasts. In Ashford's series, as in that of Boycott and Haldane, megaloblasts never predominated. Poikilocytosis was present in all Ashford's cases. In Capps'[2] case the count sank in two months from 2,576,000 to 748,000; the hæmoglobin was always relatively low (color index 0.38 to 0.88) with scanty normoblasts and no megaloblasts. At autopsy the marrow was *yellow*, *i.e.*, showed no compensatory regeneration.

In the case reported by Evans,[3] the red cells averaged 2,500,000, in Yates'[4] case they sank within a week from 2,500,000 to 800,000.

In Ashford's second series[5] of 77 cases, 130 examinations were made (excluding those when only the hæmoglobin was tested). The color index was always low, but the count of red cells fell only twice below 1,000,000.

Sandwith[6] studied in Egypt 173 cases. Of these only 3 exceeded 4,000,000 red cells per cubic millimetre; 23 per cent were found to have between 3,000,000 and 4,000,000; 46.8 per cent lay between 2,000,000 and 3,000,000, and 28.3 per cent had less than 2,000,000. His minimum count was 930,000, and his average count of hospital cases was 1,290,000 per cubic millimetre. The average of all cases is 2,420,000; the hæmoglobin, 26 per cent; the average color index 0.54 per cent.

In many of the recorded cases the abrupt rise and fall in the red cells is astonishing.

In view of all the evidence it appears that the contradictions between the statements of such writers as Boycott and Haldane, who assert that the blood resembles chlorosis, and the reports of many other writers that it resembles pernicious anæmia, depend in part upon the great variations in the severity of different epidemics. In the milder cases or in the earlier stages of any case we get counts like those of chlorosis or any other secondary anæmia of moderate grade. In severe cases, however, the count may fall as low as in average cases of pernicious anæmia. The volume index (Capps), determined by comparing the length of the packed-down column in the hæmatocrit with the count of red cells, may be high, as in pernicious anæmia (1.17 to 1.22 in Capps' case); but the *color index is low* in practically all the recorded cases, whether mild or severe (Ashford, 0.51 in 61 cases, Sandwith 0 54).

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[1] Ashford: New York Med. Jour., 1900, p. 552.
[2] Capps: Jour. Am. Med. Assn., January 3d, 1903.
[3] Evans: *Ibidem*, April 11th, 1903.
[4] Yates: Johns Hopkins Bull., December, 1901.
[5] Ashford: Amer. Med., 1903, p. 391.
[6] Sandwith: Eleventh Internat. Med. Cong., Rome, 1894.

Leucocytes.

In Boycott and Haldane's series the range was from 3,800 to 56,000; but in 16 of the severer (anæmic) cases the average was 13,600. They found that the maximum leucocytosis occurred early in the disease before the anæmia was severe. The highest counts (56,000, 44,000, 24,000, and 20,000) were all in young men with a history of from six weeks to six months' illness and with relatively slight symptoms. The lowest counts (3,800, 6,200, 6,700, and 6,800) were in cases of from two to four years' standing. In all but one of Ashford's cases (presumably more chronic), the leucocytes were normal or subnormal.

Differential Count.

The main feature, agreed upon by all observers, is the marked eosinophilia, absolute and relative. According to Boycott and Haldane the eosinophilia varies with the total leucocyte count, that it is highest in fresh, early cases occurring in young men, and less marked in the long-standing cases. It bears no close or direct relation to the degree of anæmia. The averages in sixteen anæmic cases were:

Eosinophiles	**23**	**per cent**	**or**	**3,059**	**absolutely**
Polynuclears	**48.7**	"	"	**6,477**	"
Small lymphocytes	**14.4**	"	"	**1,915**	"
Large mononuclears	**5.9**	"	"	**785**	"
Intermediate forms	**7.4**	"	"	**984**	"
Mast cells	**6**	"	"	**80**	"

In one case the mast cells were 2 5 per cent, but in 6 out of 58 cases none was found.

The detailed results of this admirable study are exhibited in the tables on page **494**.

Case.	Date.	Duration.	Red cells per cubic millimetre.	Per cent haemoglobin.	Color index.	Leucocytes per cubic millimetre.	Lymphocytes.	Intermediate forms.	Large mononuclears.	Polynuclears.	Eosinophiles.	Mast cells.	Neutrophilic myelocytes.	Absolute number eosinophiles.
1	Oct. 31	3 years...	3,216,000	48	0.74	8,800	13.4	7.4	6.2	56.2	16.0	0.8	0	1,408
	Nov. 15	....	....	43	....	....	10.8	5.6	3.4	61.0	18.0	1.2	0	
	Dec. 1	....	....	43										
2	Oct. 31	4 years...	2,192,000	35	.81	3,800	16.6	8.2	5.8	51.0	17.8	.6	0	676
	Nov. 7	....	....	....	....	....	11.8	4.4	2.2	72.0	8.8	.8	0	
3	....	4 years...	3,024,000	38	.63	6,800	16.2	11.0	10.4	50.0	11.4	1.0	0	
4	Oct. 31	4 years...	3,328,000	37	.56	8,200	16.6	5.2	5.2	53.0	19.4	.6	0	
	Nov. 20	....	....	36										
	Nov. 25	....	....	45	....	....	21.0	3.0	1.5	39.5	33.5	1.5	0	
5	....	5 years...	3,968,000	56	.71	7,500	16.6	11.8	7.8	47.0	16.8	0	0	
6	....	3 years...	3,376,000	54	.79	13,100	6.6	13.4	15.6	43.0	20.6	.8	0	2,698
7	....	2 years...	4,424,000	74	.83	10,750	26.0	6.2	7.0	54.4	6.0	.4	0	
8	....	....	4,712,000	94	1.00	12,700	31.8	9.6	5.9	36.0	17.2	.4	0	
9	....	6 years...	4,936,000	102	1.04	10,000	31.4	4.0	3.6	55.2	5.6	.2	0	
10	Nov. 5	2 months.	3,432,000	40	.58	24,400	10.0	7.6	4.2	48.4	29.0	.8	0	7,076
	Nov. 19	....	....	....	....	31,400								
11	Nov. 16	1 year...	1,533,000	17	.56	12,960	14.2	2.4	3.6	62.8	15.8	1.2	...	2,048
	Dec. 10	....	2,192,000	25	.57	12,200	7.4	2.6	3.2	74.4	11.0	.4	1.0	
	Dec. 18	....	....	36	....	7,690	18.4	....	5.2	58.0	17.0	1.4	.2	
	Dec. 20	....	....	....	....	7,850	11.0	1.8	5.2	67.0	13.6	1.4	0	
12	Nov. 20	18 months.	3,192,000	50	.78	44,000	6.3	0.5	0.7	19.5	72.7	.3	0	31,988
	Nov. 21	....	....	....	....	....	8.9	3.6	0.5	20.7	65.8	.5	0	
							9.0	3.1	0.5	20.7	66.2	.5	0	
13	....	4 years...	3,768,000	47	.63	16,200	16.8	3.6	3.0	61.6	14.6	.4	0	2,365
14	....	8 months.	3,330,000	92	1.38	13,500	20.6	3.4	1.6	45.8	27.6	1.0	0	
15	....	8 years...	4,072,000	58	.71	13,500	9.2	8.0	8.0	52.0	22.0	.8	0	2,970
16	....	4 years...	4,488,000	99	1.11	6,200	36.6	6.6	3.2	40.2	12.0	1.4	0	
17	....	3 years...	4,128,000	74	.90	12,400	27.6	18.0	6.6	43.6	3.7	.3	0	
18	....	2 years...	3,352,000	36	.53	10,700	17.5	6.5	2.8	42.5	30.1	0	0	3,231
19	....	1 year...	3,456,000	70	1.01	9,250	25.0	6.4	4.4	53.0	10.4	.8	0	11,577
20	....	2 years...	5,384,000	62	.58	9,000	37.8	7.4	2.8	38.6	12.2	1.2	0	
21	....	3 years...	5,280,000	70	.66	8,650	19.5	15.8	6.8	37.3	20.6	.16	0	
22	....	6 years...	3,272,000	89	1.37	7,600	31.0	3.8	2.8	48.2	13.8	.4	0	
23	....	9 months.	4,848,000	88	.91	8,100	33.0	4.2	3.8	47.6	11.2	.2	0	
24	....	9 months.	3,144,000	46	.74	12,300	10.6	9.0	5.4	42.8	32.0	.2	0	3,936
25	....	5 years...	3,216,000	46	.72	12,000	13.2	4.8	4.6	57.6	19.0	.8	0	
26	....	....	4,080,000	80	.98	11,100	20.2	4.2	6.8	55.6	12.6	.6	0	
27	....	5 weeks..	3,296,000	44	.67	11,600	19.0	4.2	3.8	55.6	16.6	.8	0	
28	....	....	5,112,000	100	.98	6,900	23.8	4.4	3.8	47.0	20.4	.6	0	
29	....	6 months.	4,208,000	98	1.16	20,600	21.0	4.2	1.2	16.6	56.2	.8	0	
30	....	3 years...	4,176,000	82	1.00	13,600	14.8	7.0	3.6	51.8	22.6	.2	0	
31	....	5 years...	4,706,000	66	.70	10,500	14.2	5.5	4.0	60.25	15.25	.75	0	
32	....	few weeks.	5,350,000	80	.75	56,000	5.4	5.4	2.8	25.6	66.2	0	0	37,072
33	....	2 years...	2,900,000	38	.65	6,700	27.0	15.0	7.0	36.5	14.0	.5	0	
34	....	1 year...	....	88	....	7,200	12.8	11.2	4.0	52.0	20.0	0	0	
35	....	1 year...	....	70	....	...	15.6	6.4	3.4	47.4	26.4	.9	0	
36	....	6 years...	....	58	....	....	21.6	3.0	1.4	69.8	3.6	.6	0	
37	....	2 years...	....	104	....	....	41.2	4.6	2.4	34.2	17.0	.6	0	
38	....	2 years...	....	34	....	....	15.6	3.0	1.4	55.6	24.4	0	0	
39	....	18 months.	....	36	....	....	19.0	5.2	1.6	54.0	20.2	0	0	
40	Dec. 12	3 years...	....	52	....	....	14.2	5.2	1.8	69.0	9.4	.4	0	
	Dec. 19	....	....	62	....	....	15.6	4.0	5.2	58.0	16.4	.8	0	
41	....	6 years...	....	50	....	....	15.6	6.4	3.0	58.4	15.6	1.0	0	
42	....	2 years...	....	61	....	....	12.8	7.6	3.8	64.8	10.2	.8	0	
43	....	....	....	66	....	....	13.6	10.2	5.8	62.4	7.0	1.0	0	
44	....	8 years...	....	....	....	....	27.0	9.0	1.8	48.0	13.8	.4	0	
45	....	5 months.	....	100	....	....	8.0	7.0	4.75	67.25	11.5	1.5	0	Normal
46	....	....	....	....	....	....	20.0	20.0	5.5	61.0	13.0	.5	0	240

Regarding the eosinophiles, Ashford's conclusions from 77 cases studied in Porto Rico agree in the main with those of Boycott and Haldane: *i.e.*, he finds the highest percentages in recent cases and the lowest in chronic cases. "After treatment in chronic cases and in those in the later stages of the disease a rise in eosinophiles may be expected and is of good prognostic import When, however, there is a fall in eosinophiles and no improvement in physical signs, death may often be the result." Four out of five cases that died from the anæmia had relatively low counts of eosinophiles. After the patient is cured there is a final return to the normal percentage within from three to six months.

TABLE CXI.—SCHEDULE OF BLOOD EXAMINATIONS IN NINETEEN CASES AT PONCE, PORTO RICO, BY ASHFORD.

Date.	Current number.	Red cells.	Percentage of hæmoglobin.	White cells.	Percentage of poly-morphonuclear leucocytes.	Percentage of small leucocytes.	Percentage of large leucocytes.	Percentage of eosinophiles.	Normoblasts per cubic millimetre.	Megaloblasts per cubic millimetre.	Remarks.
Nov. 4th..	1	1,530,116	20	6,800	65	21	9	5	26	13	Poikilocytosis, Polychromatophilia, many microcytes and macrocytes.
Nov. 23d..		1,880,000	16								
Nov. 3d ..	2	697,776	20	7,960	59	17	15	9	144	46	Poikilocytosis. Polychromatophilia, many macrocytes and microcytes.
Nov. 23d..		2,664,440	23								
Nov. 4th..	3	1,533,112	22	2,000	64	22	8	6	8	..	Poikilocytosis. No rouleaux.
Nov. 23d..		1,973,328	23								
Nov. 5th..	4	1,200,000	15	4,200	64	23.4	6	6.6	100	8	Poikilocytosis. Polychromatophilia.
Nov. 23d..		801,104	17								
Nov. 6th..	5	1,484,440	10	6,000	64	24	8	4	12	..	Poikilocytosis. Slight tendency to rouleaux formation; macrocytes and microcytes, latter predominate over former.
Nov. 23d..		687,776	14								
Nov. 6th..	6	2,193,328	23	8,800	65	26	8	1¼	123	35	Poikilocytosis. No tendency to rouleaux formation.
Nov. 7th..	7	1,633,328	17	5,600	60	23	5	12	11	..	Poikilocytosis. Many macrocytes and microcytes; slight rouleaux formation; marked chromatophilia.
Nov. 7th..	8	2,064,664	23	4,800	74	17	6	3	28	..	Poikilocytosis. Rouleaux formation good.
Nov. 23d..		3,084,440	31								
Nov. 7th..	9	1,271,104	14	7,800	60	17	6	17	30	15	Has elephantiasis Arabum, but I cannot identify the filaria as yet. Microcytes predominate over macrocytes. Good rouleaux formation.
Nov. 23d..		2,520,000	24								
Nov. 7th..	10	1,600,000	17	1,500	72	20	4	4	6	..	Poikilocytosis.
Nov. 23d..		668,888	13								
Nov. 8th..	11	1,800,000	25	4,600	69	22	7	2	9	..	Poikilocytosis.
Nov. 8th..	12	2,296,656	30	7,680	52	26	12	10			
Nov. 9th..	13	1,268,888	20	6,800	63	17	7	13	..	..	Poikilocytosis. Rouleaux formation good.
Nov. 9th..	14	2,440,000	25	11,000	50	10	9	31	..	..	Poikilocytosis. Rouleaux formation slight; has abscess of liver.

TABLE CXI.—SCHEDULE OF BLOOD EXAMINATIONS IN NINETEEN CASES AT PONCE, PORTO RICO, BY ASHFORD (*Continued*).

Date.	Current number.	Red cells.	Percentage of hæmoglobin.	White cells.	Percentage of polymorphonuclear leucocytes.	Percentage of small leucocytes.	Percentage of large leucocytes.	Percentage of eosinophiles.	Normoblasts per cubic millimetre.	Megaloblasts per cubic millimetre.	Remarks.
Nov. 9th..	15	2,353,328	17	12,700	73	17	4	6	..	..	Poikilocytosis. Rouleaux.
Nov. 9th..	16	2,934,444	..	5,200	72	20	5	3	10	10	Tertian malarial parasites found. Rouleaux good.
Nov. 10th.	17	2,140,000	23½	18,000	40	12	8	40	36	..	Poikilocytosis. Rouleaux good. I believe this man to have been suffering from pneumonia at time of examination.
Nov. 12th.	18	Unknown.	30	9,000	60	16	10	10	125	..	Poikilocytosis. Rouleaux formation good.
Nov. 20th.	19	1,560,000	16	2,400	72	10	5	13			

These two tables, the first from a relatively mild and recent epidemic, the second from a locality where the disease has probably been endemic for years, should give, I think, a fair idea of the range of variation in different groups of cases.

The number of cases recently reported in this country is large. They are well summarized in Capps' article (*loc. cit.*) and in Stiles' monograph.[1]

Diagnostic Value.

The presence of eosinophilia in any case of anæmia should henceforth suggest the examination of the stools for uncinaria eggs. There are other parasites which produce anæmia with eosinophilia (*e.g.*, hydatids), but none is so common as the uncinaria, and since the discovery by Stiles that considerable regions of our Southern States are infested with an American species of the worm and that a form of anæmia produced by it is common among the "poor whites" of these regions, the practical importance of blood examinations has been increased.

Effects of Treatment.

Of Sandwith's 173 cases he states that the least gain on treatment was 310,000 red cells per cubic millimetre. Another case, that of a boy, gained in one month seven pounds in weight and 2,208,000 red cells per cubic millimetre. Ten patients gained over 2,000,000, one of them 2,542,000. His average gain of all cases in hæmoglobin was from 22 to 32 per cent.

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[1] Stiles: "Report on the Prevalence and Distribution of Uncinariasis in the United States." Hygienic Laboratory, Bulletin No. 10, February, 1903.

Agnoli[1] reports a case in which there was a gain of 2,168,000 red cells per cubic millimetre and of twenty-six pounds in weight in thirty-five days. Eighty-five of Ashford's one hundred cases completely recovered.

TRICHINIASIS.

In March, 1896, a case of trichiniasis entered Professor Osler's wards at the Johns Hopkins Hospital. The study of the blood of this case by Thomas R. Brown was the means of calling the attention of the profession for the first time to the value of blood examination in the diagnosis of trichiniasis. The blood was examined daily for over two months. The total leucocyte count gradually rose from 17,000 at entrance to 35,700 forty-four days later. Thence it declined until, on the sixty-eighth day, it was 11,000. The eosinophiles were 37 per cent (6,300 absolute) at entrance, and rose with the total count until a percentage of 54 (19,500 absolute) was reached on the forty-fourth day (when the total leucocytes were 35,700). The highest percentage (68.2) was reached on the forty-ninth day, when the leucocytes were 17,700 (eosinophiles 11,070 absolute). On the sixty-eighth day (the date of discharge) the eosinophiles were 68 per cent (1,850 absolute).

A year later Brown studied a second case. His examinations showed as before a very marked eosinophilia (see table CXII.).

TABLE CXII.—CASE II.—BLOOD CHART.

DATE.	Leucocytes.	PERCENTAGE OF THE VARIOUS FORMS OF LEUCOCYTES.				TOTAL NUMBER OF VARIOUS FORMS PER C.MM.			
		P. N. Neut.	L. M. and T.	S. Monos.	Eos.	P. N. Neut.	S. Monos.	L. M. and T.	Eos.
April 15th..	13,000	43.1	6.5	1.4	42.8	5,600	180	840	5,560
16th..	....	47.7	4.7	4.5	39.1				
17th..	....	52.0	2.8	7.6	37.6				
18th..	8,000								
19th..	....	57.2	2.8	8.0	32.0				
20th..	8,900	55.2	3.8	11.2	31.8	4,900	1,000	340	2,830

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[1] Agnoli: "Consideraciones sobre dos casos de anemia por Ankylostoma duodenal." La Cronica Medica, Lima, Peru, 1898, vol. x., p. 6.

TABLE CXII.—CASE II.—BLOOD CHART (*Continued*).

DATE.	Leucocytes.	Percentage of the Various Forms of Leucocytes.				Total Number of Various Forms per C.mm.			
		P. N. Neut.	L. M. and T.	S. Monos.	Eos.	P. N. Neut.	S. Monos.	L. M. and T.	Eos.
April 21st..	8,700								
22d...	10,700	58.0	2.7	11.7	27.7	6,200	1,250	290	2,960
23d...	6,000	56.2	2.0	15.2	26.2	3,370	910	120	1,570
24th..	11,000	60.4	4.0	13.2	22.4	6,640	1,450	440	2,460
25th..	11,000	57.2	4.2	18.6	20.0	6,290	2,050	460	2,200
26th..	9,600	60.7	5.3	12.3	21.7	5,830	1,180	510	2,080
27th..	11,300	63.0	5.0	17.0	14.7	7,120	1,920	560	1,660
28th..	12,700	62.7	4.0	17.0	16.3	7,960	2,160	510	2,070
29th..	12,000	67.0	3.25	15.25	14.0	8,040	1,830	390	1,680
May 1st...	10,700	58.3	4.0	22.0	15.7	6,240	2,350	430	1,680
3d...	13,000	64.3	4.0	16.0	15.7	8,360	2,080	520	2,040
5th..	12,000	64.7	4.0	16.0	15.3	7,760	1,920	480	1,840
7th..	9,300	62.8	4.0	16.4	16.8	6,140	1,530	370	1,560
10th..	10,700	60.4	2.8	16.4	20.0	6,460	1,750	300	2,140
12th..	11,000	60.4	3.3	16.6	19.6	6,640	1,820	360	2,160
14th..	12,000	58.8	2.8	18.8	19.6	7,060	2,260	340	2,350
17th..	9,000	58.8	3.6	20.0	17.6	5,290	1,800	320	1,580

Brown's third case was studied in December, 1897.

The blood (Table CXIII.) on admission showed forty-five per cent of eosinophiles, and this, as in the two previous cases, led to the diagnosis of trichiniasis and the subsequent confirmation of that diagnosis by the removal of a portion of muscle and the discovery of trichinæ therein.

TABLE CXIII.—CASE III.—BLOOD CHART.

Date.	Red blood corpuscles.	Leucocytes.	Per cent polymorphonuclear neutrophiles.	Per cent large mononuclears and transitional.	Per cent small mononuclears.	Per cent eosinophiles.
Dec. 22d ..	......	....	48.4	4.7	1.5	45.4
23d ..	......	17,000	52.7	3.6	3.1	40.4
27th ..	4,700,000	15,300	42.4	4.0	5.6	45.0
Jan. 3d...	4,300,000	12,000	42.2	4.2	4.6	49.0
7th ..	......	14,700	31.6	4.4	19.0	44.6
10th ..	4,546,000	......	32.4	3.0	21.8	42.8
14th ..	......	13,000	35.2	4.0	23.4	87.2
22d...	......	9,000	45.5	2.0	17.7	34.7

This case was seen subsequently (July 10th, 1898) six months after the disappearance of all symptoms, and the following (*normal*) count was registered.

The count made on July 10th, 1898, was:

Leucocytes (per cubic millimetre.)	7,000
Polymorphonuclear neutrophiles	68 per cent.
Small mononuclears	23 "
Large mononuclear and transitional forms	6 "
Eosinophiles	3 "

A fourth case was reported by the same writer in January, 1899 (*Medical News*). The counts were as follows:

Date, 1898.	Leucocytes.	Per cent polymorphonuclear neutrophiles.	Per cent small mononuclears.	Per cent large mononuclears and transitionals.	Eosinophiles.
August 8th	18,100				
10th	......	....	....	....	48
13th	......	43	7.8	1.7	48
28th	8,200	45	14.5	2	38.5
September 4th	7,900	49	18.5	2.5	30
18th	......	55.2	19.6	2	23.2
25th	9,600	61.5	16	2.5	20
October 2d	8,750	54	19.5	2.5	24
November 5th	......	49	40	2.5	8.5
13th	......	64.5	27	3	5.5
20th	......	61	27	4.5	7.5

In January, 1900, Blumer[1] and Neumann report a "Family Outbreak of Trichinosis" including nine cases. The counts were as follows:

Name.	Date.	Leucocytes.	Per cent polynuclears.	Per cent transitionals and large mononuclears.	Per cent small mononuclears.	Per cent eosinophiles.
Case 1. D. V.	March 8th	19,000	47.4	8.8	3.2	40.6
	13th	18,000				
	19th	12,400	50.6	4.4	7.6	37.4
	26th	20,600	69.6	5.6	10.0	14.8
	April 1st	13,200	73.0	5.0	12.0	10.0
Case 2. Mary C.	March 8th	8,400	61.4	6.8	10.0	21.8
	12th	20,000	51.6	10.4	14.6	23.4
	19th	17,200	39.0	4.8	16.2	40.0
	26th	12,000	48.0	6.6	14.6	30.8
	April 1st	16,000	42.0	4.3	12.2	41.5
Case 3. A. V.	March 8th	24,000	56.8	6.4	3.6	33.3
	12th	14.000	52.4	3.8	7.8	36.0
	19th	20,600	64.4	2.8	5.2	27.6
	26th	18,000	66.25	4.0	6.5	23.25
	April 1st	15,200	56.6	4.4	10.4	28.6
Case 4. Mrs. D. V.	March 8th	8,000	51.0	7.8	7.6	33.6
	12th	......	50.8	4.2	18.0	27.0
	19th	12,400	50.6	5.6	11.0	32.8
	26th	13,200	54.0	5.0	11.0	30.0

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[1] American Jour. of the Med. Sciences.

Name.	Date.	Leucocytes.	Per cent polynuclears.	Per cent transitionals and large mononuclears.	Per cent small mononuclears.	Per cent eosinophiles.
Case 5. T. V.......	March 8th	8,000	32.6	10.8	6.4	50.2
	12th	14,000	49.0	4.2	15.0	31.8
	19th	18,600	41.4	5.6	10.8	42.2
	26th	14,600	35.0	3.5	18.5	43.0
Case 6. R. G.......	March 9th	14,000	45.6	15.16	7.0	32.16
	19th	17,200	45.4	2.6	6.0	46.0
	26th	8,000	48.8	5.0	10.8	35.4
	April 9th	6,000	64.4	6.8	12.2	16.6
Case 7. J. V.......	March 12th	16,000	44.0	9.2	15.8	31.0
	19th	23,000	53.2	2.8	6.2	37.0
	26th	16,600	41.6	6.0	13.0	39.4
	April 1st	8,600	39.3	9.0	16.1	35.6
Case 8. R. V.......	March 12th	10,000	39.0	6.0	20.0	35.0
	19th	14,600	36.0	4.8	8.5	50.4
	26th	12,600	55.5	5.5	9.25	29.75
	April 1st	12,600	44.0	7.0	5.5	38.0
Case 9. Mrs. R. G.	March 9th	12,400	48.0	9.6	25.4	17.0
	19th	15,200	59.2	4.0	16.8	20.0
	26th	12,600	67.0	6.5	13.0	13.5
	April 9th	10,000	74.0	5.0	13.0	8.0

My own experience is as follows:

Case.	Date.	Red cells.	White cells.	Per cent haemoglobin.	Per cent polynuclear.	Per cent lymphocytes.	Per cent eosinophiles.	Per cent mast cells.	Per cent myelocytes.
1.............	September 30th, 1897.	5,120,000	11,000	..	39.0	31.0	28.0	2.0	
	November 4th.........	4,900,000	7,000	..	36.5	46	17	.5	
2.............	September 6th, 1899..	......	1,410	..	59	3	34	2	2.0
	10th......	......	25,000						
	13th......	......	23,000						
	15th......	......	21,000	..	71.2	7	19	2	.8
	19th......	......	11,000						
	22d......	......	14,000						
2.............	September 29th......	4,712,000	10,900	70	71.2	9.6	16	2.0	1.2
	November 4th........	......	......	..	53.6	23	23	.4	
	10th.......	......	......	..	58.9	32	9.1		
	29th.......	......	......	..	67.8	24.4	7.8		
3.............	First day..............	......	15,600	..	65	11	22	1.4	6
	Fourth day...........	5,728,000	11,600	..	60	16	24		
	Seventh day..........	......	10,500	..	75	18	7		
	Tenth day............	......	13,200	..	39	23	37	.6	4
	Thirteenth day.......	......	16,100	..	52	13	35		
	Fifteenth day........	......	15,200	..	39	37	23	1	
4..........	....	......	17,900	..	54	22	24		

Atkinson[1] reports one case as follows:

Date.	Red cells.	White cells.	Per cent haemoglobin.	Per cent polynuclear.	Per cent lymphocytes.	Per cent eosinophiles.
January 14th, 1899....................	....	......	..	31.1	9.5	58.5
18th..........................	5,528,000	28,000	93	21.5	24.2	54.3
25th..........................	....	......	..	25.6	39.4	35
31st..........................	....	....	..	43.4	16.6	40

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[1] Phila. Med. Journal, June 3d, 1899.

Gwyn[1] reports a similar case in which the eosinophiles ranged from 33 to 65.9 per cent during a period of six weeks. The leucocytes were at one time 17,000 per cubic millimetre

Stump[2] found 52 per cent of eosinophiles in his case.

W. W. Kerr[3] puts the following figures on record:

	Date. 1899.	Red cells.	White cells.	Per cent hæmoglobin.	Per cent polynuclear.	Per cent small lymphocytes.	Per cent large lymphocytes.	Per cent eosinophiles.
Case 1..	Nov. 9th	5,800,000	25,000	..	52.0	1.0	1.0	42.0
	10th	4,888,000	20,600	85	49.4	3.6	2.8	44.2
	11th	....	......	..	53.6	5.9	2.2	38.3
	13th	....	......	..	41.7	4.3	..	54.0
	15th	....	......	..	36.6	7.7	3.2	52.0
	16th	....	......	..	35.0	5.3	7.6	52.5
	17th	....	13,000	..	47.0	8.5	15.5	29.0
	18th	....	......	..	46.5	10.5	10.9	31.1
	20th	....	......	..	48.0	8.0	8.0	34.0
	22d	....	......	..	50.8	2.0	14.0	32.0
	23d	....	......	..	52.4	10.9	6.8	38.3
	27th	....	......	..	40.0	15.0	4.0	41.0
	29th	4,250,000	10,000	100	22.5	19.8	14.6	43.0
	Dec. 3d	....	......	..	28 7	2.8	10 6	57.8
	8th	....	......	..	10.6	6.0	14.8	68.7
	11th	....	......	..	23.6	13.2	14.3	48.9
	13th	....	......	..	23.9	9.8	5.6	60.7
Case 2..	Nov. 17th	....	......	..	41.6	16.4	23.9	18.1
	18th	....	......	..	53.2	18.9	6.0	21.9
	20th	....	......	..	37.0	11.0	6.0	45.0
	21st	....	......	..	34.0	11.0	4.0	50.0
	22d	....	......	..	20.0	8.2	3.2	68.0
	23d	....	......	..	15.3	5.7	2.1	76.9
	24th	....	......	..	10.4	7.2	1.4	81.0
	25th	....	......	..	10.5	6.4	2.4	80.7
	27th	3,340,000	20,000	77	17.0	6.4	9.1	66.9
	29th	....	......	..	6.5	3.9	8.4	81.2
	Dec. 1st	....	......	..	4.2	3 0	6.1	86.6
	2d	....	.... .	..	11.4	10.1	4.9	73.5
	3d	....	......	..	10.0	7.3	6.1	76.6
	5th	....	......	..	14.8	8.0	7.0	70.2
	6th	....	......	..	0.75	5.0	18.8	76.0
	8th	....	......	..	3.1	9.5	8.6	78.8
	9th	....	......	..	10.9	3.6	9.0	72.7
	11th	....	......	..	11.2	18.2	14.2	56.4
	13th	3,300,000	17,000	..	13.1	9.4	9.3	68.2

Harlow Brooks[4] examined the blood in one case, and found at the time of admission to the Bellevue Hospital (February 2d, 1900)

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[1] Centralbl. f. Bakt., vol. xxvi., No. ii.

[2] Phila. Med. Jour., June 17th, 1899

[3] Phila. Med. Journal, August 25th, 1900.

[4] Med. Record, May 19th, 1900.

18,000 leucocytes, with 10 per cent of eosinophiles; on February 12th, 1900, 44 per cent of eosinophiles; thence a steady increase up to 83 per cent, followed by a decline, until on March 14th 15 per cent of eosinophiles was present. Many of the granules were smaller than those of normal eosinophiles, but there was no evidence of forms transitional between eosinophiles and neutrophiles.[1]

F. P. Kinnicutt[2] reported a similar case, and H. C. Gordinier[3] mentions two, one presenting 77 per cent, the other 29.9 per cent of eosinophiles.

In one of my cases, when the symptoms disappeared, the eosinophiles gradually returned to normal. Two years later a relapse occurred—not a reinfection—and the eosinophiles became increased as before—later decreasing again as the patient recovered from this recrudescence of the disease.

Summary.

In active cases eosinophilia is the rule. It probably occurs during some part of the course of all infections, but in those of long standing or quiescent it may disappear. With a recrudescence of the disease the eosinophilia may reappear, its duration depending probably on the degree of activity of the reactive process in the muscles.

Diagnostic Value.

The characteristic blood lesions change trichiniasis from the position of a disease very difficult and uncertain of diagnosis (without excision of a bit of muscle) to one whose recognition is usually easy. Cases formerly diagnosed as typhoid, muscular rheumatism, or neuritis now find their true interpretation.

STRONGYLOIDES INTESTINALIS.

Teissier[4] reports finding the embryos of this nematode in the blood of a patient in Guiana whose stools swarmed with the same organism. Bücklers has recorded the following data:

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[1] Many additional cases supporting these have been reported in 1901 and 1902. Drake (Journal Med. Research, 1902) and Da Costa (*Loc. cit.*, p. 435) have shown that it is possible, though exceedingly rare, to have trichiniasis without eosinophilia. Very possibly it may be true that in long-standing cases the eosinophilic reaction dies out as it does in uncinariasis.

[2] Practitioners' Soc., February 2d, 1900.

[3] Medical Record, October 20th, 1900.

[4] Teissier: Comp. rend. d. l'Acad. des Sciences, 1895, No. 3.

STRONGYLOIDES INTESTINALIS.

	Per Cent.
Eosinophiles	13.5
Polynuclears	38.5
Lymphocytes and transitional	48

STRONGYLOIDES INTESTINALIS WITH UNCINARIA.

Eosinophiles	15
Polynuclears	58
Lymphocytes and transitionals	27

P. K. Brown[1] in a case of strongyloides intestinalis with autopsy reports: (*a*) Red cells, 3,882,000; white cells, 9,400; hæmoglobin, 65 per cent; polynuclears, 71.3 per cent; lymphocytes, 22.3 per cent; eosinophiles, 6.3 per cent. (*b*) Strongyloides with uncinaria and tricocephalus: Leucocytes, 7,000; eosinophiles, 5 per cent. (*c*) Strongyloides with uncinaria and tricocephalus: Leucocytes, 7,600; eosinophiles, 10 per cent.

The following data are from Büklers:

	Case I. Oxyuris and ascarides.	Case II. Oxyuris.	Case III. Oxyuris with ascarides and trichocephalus.	Case IV. Oxyuris with ascarides, trichocephalus and Tænia saginata
Eosinophiles	19 per ct.	16 per ct.	8 per ct.	5.7 per ct.
Polynuclears	53 "	63 "	69 "	63.3 "
Lymphocytes and transitionals	28 "	21 "	23 "	31.0 "

TABLE CXIV.—ASCARIDES (alone).

	Case I.	Case II.	Case III.	Case IV.
Eosinophiles	7.4 per ct.	8.5 per ct.	9.8 per ct.	1.8 per ct.
Polynuclears	55.0 "	55.0 "	50.0 "	
Lymphocytes and transitionals	37.6 "	26.5 "	40.2 "	

Longridge (*Brit. Med. Jour.*, November 8th, 1902), in a case of tuberculous peritonitis with ascaris lumbricoides, records: Red cells, 4,800,000; leucocytes, 12,400; eosinophiles, 6 8 per cent.

The report of the Jenner Hospital at Berne (1890) includes the account of a case in which ascaris was present in large numbers. The blood showed but 2,480,000 red cells before the expulsion of the parasite by santonin; two weeks later the red cells were 4,200,000.

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[1] Brown: Boston Med. and Surg. Jour., May 28th, 1903.

TABLE CXV.—TÆNIA (Bücklers).

	Case I. Tænia Solium.	Case II. Tænia Saginata.	Case III. Tænia Nana.	Case IV. Tænia Saginata.	Case V. Tænia Saginata.
Eosinophiles........	8.2 p. ct.	5.5 p. ct.	7.0 p. ct.	5.0 p. ct.	10.0 p. ct.
Polynuclears........	49.4 "	65.0 "	42.0 "		
Lymphocytes and transitionals......	42.4 "	29.5 "	51.0 "		

In a case of infection of the skin, with tænia solium ("Ladrerie") Achard and Loeper[1] found eleven per cent of eosinophiles (649 absolutely). Marie and Guillain[2] in a similar case found normal blood.

In ordinary intestinal infections with tapeworm, many of which I have examined, eosinophilia is not usually to be found at the time when the patients present themselves for treatment.

TÆNIA INERMIS.

Launois[3] and Emile-Weil found eosinophilia throughout the of infection.

AMŒBIC DYSENTERY.

Amberg[4] noted in five cases the presence of eosinophilia with leucocytosis and anæmia. Futcher[5] found the average leucocyte count in 43 cases to be 10,600 with no increase of eosinophiles in "a number" of cases examined with reference to this point.

TRICOCEPHALUS DISPAR.

P. K. Brown (*loc. cit.*) reports that in twelve cases in which this parasite was the only one found in the stools the eosinophiles rarely fell below five per cent.

Ostrovsky[6] has recorded a case of fatal anæmia apparently due to this parasite.

[1] Achard and Loeper: Soc. Méd. d. Hôp., 1900, p. 867.

[2] Marie and Guillain: *Ibidem*, November 8th, 1901.

[3] Launois: Sem. Méd., November 12th, 1902.

[4] Amberg: Johns Hopkins Bull., December, 1901.

[5] Futcher: Journ. Am. Med. Assn., August 22d, 1903.

[6] Ostrovsky: Ref. in N. Y. Med. Jour., 1900, vol. 72, p. 826.

CHAPTER XIII.

DISEASES OF THE SKIN.

DERMATITIS HERPETIFORMIS.

According to Leredde, who has written extensively on the condition of the blood in this disease, the following terms are in use to designate the same actual set of facts: Dermatitis herpetiformis; Dühring's dermatosis; Polymorphous pruriginous dermatitis; Hydroa (Unna); Pemphigus vegetans (Neumann); Hallopeau's infectious dermatosis; Herpes gestationis.

In all of this he finds marked constant eosinophilia, averaging 16 per cent. At times the percentage may reach 25 or 30.

My own experience includes three cases, one diagnosed as dermatitis herpetiformis, the others as hydroa æstivale. The counts were as follows:

	Case I. Dermatitis herpetiformis.	Case II. Hydroa æstivale.	Case III. Hydroa æstivale.
Polynuclear neutrophiles..	47 per cent	40.0 per cent	34 per cent
Small lymphocytes........	25 " "	42.4 " "	43 " "
Large lymphocytes........	8 " "	8.6 " "	8 " "
Eosinophiles..............	19 " "	8.2 " "	15 " "
Myelocytes...............	1 " "		

Brown[1] reports the following figures in a case of dermatitis herpetiformis (twenty-seven years' duration):

	June 12th, 1899.	June 17th, 1899.	June 25th, 1899.	June 30th, 1899.	Sept. 5th, 1899.
Red cells.................	5,128,000	....	....	5,163,000	5,808,000
White cells..............	14,000	....	....	9,000	9.700
	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.
Polynuclear neut........	32.8	31.3	29.25	39.25	36.0
Lymphocytes............	38.0	24.4	34.5	21.5	34.4
Eosinophiles.............	29.2	44.3(!)	36.25	39.25	29.3

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[1] Soc. for Original Research, Conn., October 12th, 1899.

TABLE CXVI.—ERYTHEMA MULTIFORME.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	29	....	19,700	..	First day. Temperature, 102°; erythema nodosum and multiforme.
			20,400	..	Second day. Temperature 103°.
			12,900	..	Sixth day. Temperature 98°.
2	27	....	18,400	..	Temperature 104°.
			6,800	..	Temperature 104°, third day. Eosinophiles not +.
3	18	....	11,400	65	Nodosum.
4	43	....	9,200	70	
5	17	....	8,200	..	Temperature 102°.
6	29	....	7,000	60	August 8th. Diff. count, 500 cells: Polynuclear, 75.5 per cent; lymphocytes, 20; eosinophiles, 4.5.
					September 2d. Polynuclear, 73 per cent; lymphocytes, 25; eosinophiles, 2.
7	24	....	6,150	..	Diff. count, 425 cells. Polynuclear, 69 per cent; lymphocytes, 30; eosinophiles, 1.

HERPES TONSURANS.

Mark A. Brown[1] records this blood count: White cells, 10,700; of these, there were eosinophiles, 25.2 per cent; polynuclears, 45.6; lymphocytes, 29.2.

HERPES ZOSTER.

Sabrazès and Mathis (*Rev. de Méd.*, 1901, p. 251) studied seven cases. They found no changes in the red cells or in the hæmoglobin. There was leucocytosis increasing until the third day, then decreasing until the period of desiccation, when a slight secondary rise occurred. In two weeks the blood was normal. On the first day the counts were from 11,000 to 16,000; on the third they averaged 17,900, on the fifth, 13,000. Throughout this period there was an increase of polynuclear cells and eosinophiles with a few myelocytes. The eosinophiles reached their maximum in the desquamative period—8 to 20 per cent (800 absolutely).

Bettmann (*loc. cit.*) had previously reported eosinophilia in a single case.

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[1] In Conn. Lancet Clinic, December 22d, 1900.

ACUTE ECZEMA.

No.	Age.	Red cells.	White cells.	Per cent hæmoglobin.	Remarks.
1	22	....	15,000	95	April 3d. Diff. count, 300 cells: Polynuclear, 74.7 per cent; small lymphocytes, 16.6; large lymphocytes, 5 3; eosinophiles, 3.4. May 5th. Diff. count, 400 cells: Polynuclear, 63.7 per cent; small lymphocytes, 26; large lymphocytes, 7; eosinophiles, 3.3.
			13,200	..	May 7th.
			10,200	..	May 19th.

The above data are from a recent case at the Massachusetts Hospital. Stengel and White (*loc. cit.*) record 7.9 per cent of eosinophiles in a single case.

CHRONIC ECZEMA.

Thomas R. Brown[1] reports a case of chronic eczema, studied at the Johns Hopkins Hospital, in which three counts showed 22.6 per cent, 24 per cent, and 22.7 per cent of eosinophiles.

Zappert (*loc. cit.*) notes a similar case with 8,600 leucocytes per cubic millimetre, 9.9 per cent of which were eosinopiles (843 absolute). Bettmann (*loc. cit.*) records 45 per cent eosinophiles in a similar case.

SCLERODERMA.

Two cases in Zappert's series showed:

	Leucocytes.	Per cent eosinophiles.	
1.......................	16,690	9.4	(1,580 absolute.)
2.......................	9,000	7.7	(694 ")

PSORIASIS.

One of Zappert's cases had 8,600 leucocytes, with 9.8 per cent of eosinophiles (850 absolute). Bettmann confirms this.

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[1] Jour. of Exp. Med., vol. iii., p. 320.

PEMPHIGUS.

Reporter.	No.	Red cells.	White cells.	Per cent eosinophiles.
Zappert. ..	1	3,952,000	5,300	33.0 (1,750 absolute).
Zappert. ..	2	3,940,000	10,600	14.1 (1,500 absolute).
Zappert. ..	3	4,120,000	1,640	29.2 (4,800 absolute).
Andry	4	....	13,000	15–24 (1,750–3,120 abs.)

This is confirmed by Neusser[1] and Canon,[2] and Bettmann.[3] Brown[4] in three cases found 3 per cent (360 absolute), 5 per cent (750 absolute), and in the third, no increase. Coe[5] in one case found 50 per cent, or 6,000 absolute.

LUPUS.

Two cases (Zappert). Bettmann (*loc. cit.*) confirms.

Cases.	Red cells.	White cells.	Per cent eosinophiles.
1...............	3,224,000	9,200	12.2 (1,126 absolute).
2.................	4,250,000	9,450	7.3 (696 absolute).

DRUG ERUPTIONS.

Iodide of potash[6] eruptions have been found by two observers to be associated with eosinophilia (14 per cent).

Mercurial dermatitis,[7] and the eruptions produced by picric-acid solution[8] applied externally for a burn, have likewise produced eosinophilia (15 per cent) with the latter. Zappert has seen a similar result from the rash of *sodic salicylate,* and in Ehrlich and Lindenthal's case of *nitrobenzol poisoning* (*vide supra,* page 410) the same thing was observed.

Brown's case[4] of acute acetanilid poisoning with 12 per cent of eosinophiles (3,600 absolute), though without eruption, probably belongs in this class, as does that of von Noorden, previously mentioned (*vide supra*, page 109).

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[1] Neusser: Wien. klin. Woch., 1892, p. 41.

[2] Canon: Deut. med. Woch., 1892, p. 206.

[3] Bettman: *Loc. cit.*

[4] Brown: Maryland Med. Jour., April, 1901, and July, 1902.

[5] Coe: Amer. Med., June 28th, 1902.

[6] Lerrede: Presse Méd., 1898, No. 106. Seifert and Wurzburg: Physic.-Med. Gesellsch. February, 1902.

[7] Hoffman: Berl. klin. Woch., September 29th, 1902.

[8] Achard and Clerk: Gaz. Hebd., 1900, No. 81.

In *bullous dermatitis following vaccination* Bowen[1] records:

Case.	Red cells.	White cells.	Per cent hæmoglobin.	Per cent polynuclears.	Per cent lymphocytes.	Per cent eosinophiles.	Remarks.
1	....	......	....	63	19	18	Nov. 28th, 1899.
	5,100,000	7,400	65	71	16	13	Dec. 16th, 1900.
2	....	......	....	48	80	21	

EPIDERMOLYSIS BULLOSA HEREDITARIA.

Columbini[2] found 8 to 10 per cent of eosinophiles, and Brown[3] 97 per cent (1,100 absolute).

XERODERMA PIGMENTOSUM.

Okamura (*Arch. f. Dermat. u. Syph.*, February, 1901) notes a leucocytosis averaging over 40,000 in three cases, in two of which there was moderate eosinophilia.

DERMATITIS EXFOLIATIVA.

Pitkianen (*loc. cit.*) finds a considerable eosinophilia from the first day of the disease and contrasts the blood with that of scarlet fever in which the eosinophilia comes later and is less marked.

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[1] Bowen: Jour. of Cut. and Gen.-Urin. Diseases, September, 1901.

[2] Columbini: Monatsch. f. pract. Dermat., May 15th, 1900.

[3] Brown: Maryland Med. Journ., April, 1901, and July, 1902.

CHAPTER XIV.

THE BLOOD IN PREMATURE INFANTS.

ENGEL ("Leitfaden z. klin. Untersuch. des Blutes," Berlin, 1902) studied the blood of an embryo 23 cm. long, the heart still beating. He found: Red cells, 3,300,000; white cells, 12,500; hæmoglobin, 80 per cent (*i.e.*, notably high). There were 27,500 nucleated red cells per cubic millimetre, mostly normoblasts, with polychromatophilic protoplasm. Great variations in size and staining reactions were also present in the non-nucleated red cells.

Among the leucocytes were many myelocytes and mononuclear eosinophiles. Fischl (*Zeitsch. f. Heilk.*, 1892) believes that the eosinophiles do not enter the blood until after the seventh month of pregnancy.

THE BLOOD IN INFANCY.

I. *All the signs by which sickness is shown in the blood of adults are exaggerated in children.* Their blood is apparently more sensitive to the action of any morbid influence. Causes leading to but slight anæmia or leucocytosis in the adult produce grave anæmia and very marked leucocytosis in children. Into the reasons for this I shall not attempt to enter. The increased toxicity of their serum compared to that of adults, and the relatively recent establishment of the functions for producing and destroying blood have been suggested as explanation.

Comparatively slight hemorrhages, gastro-intestinal or respiratory disorders, which would not impoverish an adult's blood may produce considerable anæmia in a young child.

II. All forms of anæmia in infancy are apt to be associated with enlarged spleen.

III. I have already alluded to the polycythæmia and leucocytosis of the new-born, and the gradual fading out of these relative abnormalities as the child grows up. Carstanjen's[1] fine studies lead him to the following conclusions: At the moment of birth and for the next twenty-four hours, the infant's blood contains about seventy-five polynuclear cells in every one hundred leucocytes. After the first day the per cent of polynuclear cells rapidly sinks, while the lymphocytes increase, until by the sixth or ninth day of life the two forms are about equally numerous. By the twelfth day the blood has taken on the picture which it retains for the first ten months of life—*i.e.*: Polynuclears, 36 per cent; lymphocytes, 45; large mononuclears, 1; transitional forms, 18; eosinophiles 1 to 3 Mast cells and myelocytes, very scanty.

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[1] Carstanjen: Yahrb. f. Kinderh., vol. 52, 1900.

From this time on the polynuclear cells gradually rise and the lymphocytes fall until the fifth year. During the first five years Carstanjen's averages are as in the following table.[1]

Year.	Per cent polynuclear.	Per cent lymphocytes and transitionals.	Per cent eosinophiles.
One to two	42	55	3
Two to three	48	48	4
Three to four	52	43	5
Four to five	61	33	6

After this period the percentages are practically the same as in adult life.

As regards the red cells we need to remember that in the blood of the new-born there are normally very great variations in the size, shape, and staining reactions of the red cells, and that deficient rouleaux formation is the rule. Normoblasts are usually present in the earliest days of life and megaloblasts are occasionally found, but in healthy children both varieties are very scanty after the third day, and never occur after the seventh month.[2] In Warfield's cases the normoblasts averaged about 11,000 per cubic millimetre on the first day. In judgments as to the presence or absence of leucocytosis in infancy, these physiological variations are too often lost sight of, especially as the proper leucocyte count for any given infant depends not simply on its age but on the backwardness or forwardness of its development. As with the fontanels, the growth of the blood toward adult conditions may be retarded by congenital weakness (infantile atrophy, marasmus) or inherited disease (tuberculosis, syphilis) as well as by acquired sickness (rickets).

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[1] The figures of Japha (Jahrbuch f. Kinderh., 1901, vol. 53, p. 179), Karnizki (Archiv f. Kinderh., 1903, p. 42), and Warfield (Am. Med., 1902, vol. xxxvi., p. 457), are practically identical with the above. Japha found the average total leucocyte count to be 13,560 in twenty-two healthy infants under one year.

[2] Karnizki: Arch. f. Kinderheilk., 1903, p. 42.

Under the influence of any of these drawbacks a sick child's blood may be no further developed at three years than that of a healthy child of eighteen months.

IV. When we remember that in early infancy the leucocytes differ from those of adults not only in number but in that the lymphocytes are relatively more numerous ("lymphocytosis of infancy") we shall understand that any influence like rickets or syphilis, which retards development, will show lymphocytosis together with the increased leucocyte count. Qualitatively as well as quantitatively the blood reverts to a more infantile condition.

Under pathological conditions the red cells revert to the earlier type just described, and deformed or nucleated corpuscles are plentiful. This is more marked than in anæmia of the same grade occurring in adults. An anæmia that shows but thirty nucleated erythrocytes per cubic millimetre in an adult might show ten times that number in a child.

V. As I said before, all blood changes are exaggerated in infancy. This includes such physiological changes as the digestion leucocytosis or that following cold bathing, and changes in the degree of dilution or concentration of the blood seem to be similarly exaggerated, as is seen, *e.g.*, in the physiological variations in the specific gravity of the serum (Hock and Schlesinger[1]). According to Head[2] disease such as typhoid meningitis, pneumonia, or appendicitis, affect the blood of children (after the second year) exactly as they do the blood of adults.

VI. The *hæmoglobin*, though relatively high at birth and for the first few weeks, is lower than that of adults during the rest of childhood. The high percentages of the earliest weeks are not due to a polycythæmia, but to a genuine increase of hæmoglobin in the individual cells (Schiff[3]), color indexes being often over 1.

It is indispenable, therefore, that we should know the age and degree of development of a child before we can draw accurate inferences from its blood. In many of the cases reported in literature we are unable to judge whether the blood condition is pathological or not, because the age of the child is not given. For example, v. Limbeck[1] notes a case of acute gastritis reported by Fischl[2] as having an unusually high percentage of lymphocytes (59.4 per cent). But this is physiological in the first days of life, and may have been so in this case, the age not being given.

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[1] Hock and Schlesinger: Centralbl. f. klin. Med., 1891.

[2] Head: Pædiatrics, February, 1900.

[3] Schiff: Zeit. f. Heilk., vol. xi., 1890.

Observations of this sort should always represent a comparison between the conditions present *before* and *during* sickness in question.

Bearing these general considerations in mind, we shall be better able to find our way among the complications and perplexities of the blood conditions in infancy.

THE SUMMER DIARRHŒAS OF INFANCY.

Japha (*loc. cit.*) in *gastro-intestinal catarrh* (foul mucous stools and fever) found an increase in the polynuclear cells (47 to 55 per cent, normal = 42 per cent) which raised the total count to a varying extent—once to 36,000.

In *follicular enteritis* (blood and mucous stools with wasting and with or without fever) practically the same conditions obtain (polynuclears average 60 per cent; lymphocytes, 35 per cent; total count, 15,000 to 38,000).

In *cholera infantum* a higher leucocyte count occurred—51,000 to 54,000—with polynuclear 65 per cent and lymphocytes 25 per cent on the average.

Knox and Warfield[3] found practically similar results. They note also that eosinophiles are often diminished or absent in each of these groups of cases. The degree of leucocytosis seems to be of no diagnostic or prognostic value.

THE ANÆMIAS OF INFANCY.

As above mentioned, anæmic infants are apt to have enlarged spleens This may be due either to the anæmia or to some disease accompanying or underlying the anæmia (*e.g.*, rickets, syphilis). It seems more probable that the hypertrophy is not directly or exclusively dependent on the anæmia, inasmuch as similar blood changes are found without splenic enlargement. By far the greater number of reported cases of severe infantile anæmia are accompanied or caused by such diseases as rickets and hereditary syphilis, both of which may cause splenic hyperplasia even when no anæmia is present. It seems probable that the anæmia and the enlargement of the spleen are alike symptomatic of an underlying disorder.

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[1] v. Limbeck. *Loc. cit.*, p 373.

[2] Fischl: Zeit. f. Heilkunde, 1892.

[3] Knox and Warfield: Johns Hopkins Bull., July, 1902.

It does not seem to me that we can recognize in the blood of infants any of the well-defined types of anæmia which we have learned to correlate in adults with a definite set of symptoms and a definite prognosis. All such distinctions as pernicious anæmia, secondary anæmia, splenic anæmia, or chlorosis are blurred in infancy. A blood which in adult life would mean pernicious anæmia, and so death in ninty-nine per cent of the cases, is compatible with a speedy and permanent recovery in infancy.

In the midst of this confusion we may note the following praiseworthy efforts to secure order.

1. Some writers (*e.g.*, Luzet[1]) divide the anæmias of infancy into two classes: those with splenic enlargement and those without it. Luzet considers that the former class is severer than the latter and more apt to show large numbers of nucleated red corpuscles than those with normal-sized spleens. This classification, however, does not always hold. We may have very severe anæmia without splenic enlargement and splenic enlargement with slight anæmia, and the presence or absence of numerous nucleated red corpuscles is governed by conditions other than the size of the spleen.

2. Another classification of children's anæmias was proposed in 1892 by Monti and Berggrün ("Die chronische Anämie im Kindesalter," Leipsic, 1892). They divided the cases into the *mild* and the *grave*, each group being subdivided into those with leucocytosis and those without it.

$$\text{Secondary anæmia of infancy} = \begin{cases} \text{Mild} = \begin{cases} \text{With leucocytosis.} \\ \text{Without leucocytosis.} \end{cases} \\ \text{Grave} = \begin{cases} \text{With leucocytosis.} \\ \text{Without leucocytosis.} \end{cases} \end{cases}$$

They rightly discard the term "splenic anæmia," corresponding as it does to no single set of blood changes. The above classification puts pernicious anæmia, leukæmia, and anæmia infantum pseudoleukæmica (v. Jaksch) in a different category.

(*a*) Mild cases of secondary anæmia show no deformities in the shape or size of the red cells. The color index may or may not be low. The cases with leucocytosis are much more numerous than those without it and more apt to have a low color index; in other words, the loss of corpuscle substance is greater and the cases are approaching the imaginary boundary between "mild" and "grave."

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[1] Luzet: Diss., Paris, 1891.

(*b*) The grave cases have poikilocytosis, and of course a greater reduction of corpuscle substance.

"Chlorotic" conditions, and most but not all those with enlarged spleen, come under this heading; also most of those due to hereditary syphilis, prolonged diarrhœa, and rickets.

In 1894 Monti[1] gave the following classified lists of the commonest antecedents of secondary anæmia in infancy:

1. Congenital, due to...
   - Syphilis,
   - Tuberculosis,
   - Malaria, etc.

   In the mother during pregnancy.
2. Acquired..
   1. Hemorrhage.
      - From navel.
      - After circumcision.
      - Scurvy, purpura, hæmophilia, Werlhof's disease, melæna.
   2. Other causes.
      - Inanition.
      - Bad hygiene (lack of light, air, etc.).
      - Post-febrile.
      - Nephritis, diarrhœa, serous effusions.
      - Syphilis.
      - Rickets.
      - Suppuration.
      - Diseases of liver, spleen, bone, or lymph glands.

He points out that cases with leucocytosis are usually graver than those without it and may develop into pernicious anæmia; also that the presence of leucocytosis does not point to malignant disease, suppuration, or any of the causes which usually account for it in adults.

Grave cases with leucocytosis in infants under twelve months are apt to develop into the anæmia infantum pseudoleukæmica, or into true leukæmia or pernicious anæmia.

On the whole, the division of Monti and Berggrün seems much better than that according to the particular causes, *e.g.*, "rachitic anæmia," "syphilitic anæmia," etc., for there is no particular set of blood changes that follows rickets, syphilis, or any other disease. In connection with various diseases of infancy, and particularly with those last named, we may have anæmia of any grade of severity, from that reducing the red cells to 4,000,000 down to cases with only 500,000 red cells per cubic millimetre or even less. The worse the case is the more likely is it to be accompanied by leucocytosis and the more numerous will be the nucleated red corpuscles, always more numerous here than in anæmia of adults.

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[1] Wiener med. Woch., 1894.

In *syphilis*, hereditary or acquired, the red cells may fall below 1,000,000 and the leucocytes may rise as high as 58,000 (Loos). The hæmoglobin may be proportionally diminished, or may be even lower than the percentage of red cells, so that a "chlorotic" condition obtains.

Such cases have been called *chlorosis*, but it seems better to confine this term to anæmia of unknown origin and favorable course occurring in women soon after puberty, since obviously secondary cases may have similar blood.

Rickets in a case observed by v. Jaksch caused a fall of the red cells to 750,000, and Luzet counted 1,590,000 in a similar case. The hæmoglobin is usually low, but Hock and Schlesinger found 60 per cent with 2,300,000 red cells, a color index of 1.2+.

Leucocytosis may occur even when no anæmia is present. Hock and Schlesinger found 45,000 leucocytes in a rachitic child of sixteen months, sound in other respects and not anæmic. *Acute gastritis* causes at first only leucocytosis (with increased percentage of lymphocytes). If it becomes chronic the reduction of red cells is severe. Hayem found only 685,000 red cells per cubic millimetre in an infant of two months, though recovery eventually took place.

In *tuberculosis* of the lungs and peritoneum in a child of seven, Monti and Berggrün counted 3,230,000 red and 17,200 white cells with 52 per cent of hæmoglobin.

Qualitative Changes.

The exaggeration characteristic of all blood changes in infancy extends to the presence of nucleated red corpuscles, which in all forms of infant's anæmia are very numerous. What has been described on page 85 as the typical megaloblast, a large pale-stained nucleus in a very large cell (see Plate IV.), is relatively rare in infancy. The nuclei are almost always stained whatever their size, and apt to be small. Dividing nuclei are very common, both by karyolysis and karyokinesis. These changes are most often found in the anæmias of the severest type and those which resemble leukæmia (see page 525), but may occur in any marked secondary anæmia. Polychromatophilic and "degenerative" changes are very common in severe cases.

The increased leucocyte count, so frequently found, is often made up of a majority of lymphocytes. This change, as above said, is not characteristic of rickets, syphilis, or any other cause of anæmia, but it is to be regarded as a mark of the arrest of development or reversion to an earlier type of tissues brought about by various diseases in early infancy. Sometimes the large lymphocytes and sometimes the small are in excess, and for a time the blood may simulate closely that of lymphatic leukæmia, as the following cases illustrate.

No.	Age.	Sex.	Red cells.	White cells.	Per cent hæmoglobin.	Per cent polynuclear.	Per cent small lymphocytes.	Per cent large lymphocytes.	Per cent eosinophiles.	Per cent myelocytes.	Normoblasts.	Megaloblasts.	Number cells counted.	Remarks.
1	1	.....	1,836,000	65,000	12	20.6	78.1	......	0.2	1.1	34	0	500	March 13th
				78,000	....	19.1	80.	......	.3	.6	54	..	500	March 22d
				88,000	....	14.2	84.	......	.2	1.6	48	2	500	March 31st
2	Inf.	.....	4,300,000	31,000	60	57.5	26.	15.0	.5	1.0	11	89	......	July 14th
												17	1,000	July 19th
3	1⅙	Male	2,500,000	22,000	....	29.4	46.2	7.6	6.2	10.0	21	50	500	Death

The cases in the following table (from Fowler: *Brit. Med. Jour.*, September 6th, 1902) are tabulated in the order of their severity. The splenic enlargement was present in all cases and rickets in all but two; but Morse has shown that similar blood changes may occur with no splenic enlargement (see page 522). Four of the patients died with bronchopneumonia, three recovered, and the result of the rest is uncertain.

Poikilocytosis was slight, but variations in size and in staining reaction were common and marked. Megaloblasts were found in 13 of the 20 cases, but never exceeded one-quarter of the number of normoblasts. Contrary to the rule in the anæmia of adults, nucleated red cells are here numerous even in some of the mild cases. In 16 of the cases the average percentage of small lymphocytes was 26; large lymphocytes, 21; and transitionals, 12.3. "Transitional neutrophiles" (see page 102) were present in all cases.

TABLE CXVII.—ANÆMIA IN INFANTS.

No. of case.	Sex.	Age, in months.	Date.	Red corpuscles.	Hæmoglobin.	Leucocytes.	Color index.	Ratio of whites to reds.	Per cent lymphocytes.	Per cent polymorphonuclears.	Per cent eosinophiles.	Per cent myelocytes.	Nucleated reds per cubic centimetre.
1	M.	26	February 28th....	1,146,000	20	8,600	0.8	1 to 131	50.0	46.2	1.6	2.2	1,376
			March 22d........	1,540,000	25	8,900	.8	1 to 175	59.6	34.8	1.0	4.6	567
			April 27th........	1,903,000	32	8,125	.8	1 to 238	57.0	37.0	.2	5.8	1,100
			May 26th.........	1,525,000	....	10,900	....	1 to 140	59.6	28.7	1.8	10.0	544
			June 16th	2,075,000	....	5,900	....	1 to 351	69.0	28.0	.8	2.2	371
2	M.	11	....	2,200,000	30	12,000	.7	1 to 183	66.0	31.4	.8	1.0	576
3	F.	16	....	2,360,000	38	14,000	.6	1 to 181	68.8	28.8	2.0	.4	175
4	F.	11	February 11th....	1,156,000	....	32,500	....	1 to 51			....		
			February 23d.....	2,040,000	27	25,700	.6	1 to 79	49.0	49.0	.4	1.6	2,313
			March 2d.........	2,920,000	30	23,200	.5	1 to 125					
			March 10th	2,660,000	30	18,400	.6	1 to 144	61.5	32.5	3.0	3.0	1,300
			April 4th.........	2,800,000	18	45,000	.3	1 to 62					
5	F.	11	February 17th....	2,640,000	....	35,200	....	1 to 75					
			February 25th....	3,160,000	27	27,700	.4	1 to 114	62.0	34.0	.2	3.0	1,600
			March 1st.........	3,180,000	30	20,000	.5	1 to 159					
			March 9th.........	2,600,000	35	22,900	.6	1 to 112	69.0	23.2	.8	4.0	2,770
6	M.	16	September 25th...	2,630,000	....	22,600	....	1 to 115	67.2	30.4	.4	2.0	790
			October 2d........	2,900,000	....	21,600	....	1 to 134	64.0	33.0		3.0	720
7	M.	16	June 30th.........	2,500,000	....	40,000	....	1 to 62					
			November 26th ...	3,537,000	....	16,300	....	1 to 216	56.0	35.0	7.0	2.0	1,533
			December 1st.....	4,000,000	60	21,800	.7	1 to 181					
			December 12th...	3,650,000	60	21,800	.8	1 to 166	52.0	37.2	7.4	2.4	1,090
			December 29th...	4,200,000	68	17,500	.7	1 to 240					
			March 3d.........	4,940,000	72	12,600	.8	1 to 383	58.0	37.0	4.0	1.0	Few
8	M.	13	August 8th......	2,800,000	36	9,800	.6	1 to 286	70.2	25.5	.3	3.5	466
			November 11th...	3,250,000	38	12,600	.6	1 to 290	65.0	30.6	.4	4.0	540
			January 8th......	4,800,000	....	10,100	....	1 to 406	56.0	42.4	1.0	.6	126
			February 13th....	4,216,000	58	9,800	.7	1 to 430					
			March 24th.......	3,880,000	....	11,000	....	1 to 352					
			June 24th........	3,510,000	58	6,300	.8	1 to 557	52.6	42.4	.4	4.6	327
9	M.	24	....	2,370,000	....	5,800	....	1 to 408	47.2	51.0	.8	1.0	150
10	F.	10	March 27th.......	3,100,000	45	17,000	.7	1 to 182	63.0	35.8	.5	1.0	1,700
			January 15th.....	4,800,000	70	10,100	.8	1 to 475	51.2	48.0	.8		40
11	F.	11	....	3,452,000	35	23,900	.5	1 to 144	38.0	59.0	1.2	1.8	1,300
12	M.	18	....	3,800,000	46	35,200	.6	1 to 108	38.3	59.0	.2	2.5	905
13	F.	15	May 30th.........	3,960,000	57	27,000	.7	1 to 146	65.0	30.0	.5	4.5	964
			June 16th........	3,410,000	47	19,600	.6	1 to 174	58.8	38.0	1.0	2.4	1,460
14	M.	15	....	4,000,000	66	19,600	.8	1 to 200	54.6	44.2	.6	.6	138
15	F.	26	....	4,000,000	....	12,000	....	1 to 333	56.0	34.0	2.0	8.0	1,340
16	F.	21	....	4,100,000	50	12,800	.6	1 to 320	61.0	36.5	1.5	1.0	20
17	F.	13	....	4,160,000	60	11,860	.7	1 to 330	61.2	36.2	1.4	.8	512
18	F.	18	....	4,900,000	80	10,500	.8	1 to 446	55.8	43.8	.4	....	30
19	F.	18	....	4,940,000	65	10,266	.6	1 to 490	62.8	35.4	1.6	.2	20
20	M.	13	....	5,020,000	70	15,300	.7	1 to 330	57.0	40.0	2.0	1.0	612
								Average	59.1	36.9	1.2	2.8	

A further qualitative change already alluded to (see page 111) is the occurrence of *myelocytes*. We have seen that small percentages of these cells are not uncommonly seen in the anæmias of adults. Now this, like all other blood changes, is exaggerated in infancy. Myelocytes are more apt to appear and in greater numbers. Their presence is not characteristic of any one disease, but they are commonest in the severer types of secondary anæmia, such as those following syphilis and rickets. Their significance is about the same as that of normoblasts.[1] At times, however, they are so numerous as to make us hesitate somewhat before we exclude splenic-myelogenous leukæmia.

This brings us naturally to the discussion of *the difficulty of distinguishing the different blood diseases in infancy*, which naturally centres in the question of the existence and nature of the so-called

"ANÆMIA INFANTUM PSEUDOLEUKÆMICA."

Von Jaksch's[2] description of this disease (which he was the first to recognize) includes the following elements:

1. Grave anæmia—*e.g.*, 820,000 red cells per cubic millimetre in one case.
2. Extensive leucocytosis—*e.g.*, 54,660 white cells per cubic millimetre, in the same case.
3. Great variations in the form, size, and staining of the white cells.
4. Deformed, degenerated, and nucleated red cells.

This description was given by v. Jaksch[2] in 1889. He stated the relation of white to red corpuscles as 1: 12, 1: 17, and 1: 20 in the cases seen by him. Later he reported three cases in one of which the white cells numbered 114,150 and the red 1,380,000. The differential counts are not carefully given.

Almost at the same time Hayem[3] reported a similar case, and noted the abundance of nucleated red corpuscles many of which were undergoing mitosis. This was verified by Luzet,[4] who reported two cases in May, 1891 (*Arch. gén. de Méd.*); but although Luzet continues to use the name suggested by v. Jaksch, he describes the disease so differently that it is difficult to see why the same title should be given to it. He agrees with v. Jaksch in thinking that it is not simply a severe secondary anæmia due to syphilis, rickets, tuberculosis, or infectious disease.

Somewhat similar cases had already been described by various

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[1] Weil and Clerc (Rev. Mens. d. Mal. a l'Enfance, No. xxi., 1902) have put together a number of cases from their own and others' experience, showing that splenic enlargement and myelocytes in the blood are of frequent occurrence in the anæmias of infancy. They attempt quite unsuccessfully to build up from these data a new clinical entity.

[2] Von Jaksch: Wien. klin. Woch., 1889, Nos. 22, 23.

[3] Hayem: Gaz. des Hôpitaux, 1889, No. 30.

[4] Luzet: Diss., Paris, 1891.

Italian writers (*e.g.*, Fede) under the title of "*Infective Splenic Anæmia of Infants.*" Baginsky,[1] Senator,[2] Fischl,[3] Andeoud,[4] Monti and Berggrün,[5] Felsenthal,[6] Raudnitz,[7] Epstein,[8] Alt and Weiss,[9] Hock and Schlesinger,[10] Crocq,[11] and Rotch,[12] have written upon the subject, and hardly any two have described the same set of facts or agreed as to the meaning of the term.

The chief importance of the heterogeneous group of cases which have received the name of *anæmia infantum pseudoleukæmica* seems to me to be as a proof of the difficulty of distinguishing the various blood diseases in infancy. Among the cases reported under this name are some which might be any one of the following list: Pernicious anæmia, secondary anæmia with leucocytosis, Hodgkin's disease, lymphatic leukæmia, and probably splenic-myelogenous leukæmia.

(*a*) Rotch and Ladd[13] have reported a case occurring in an infant ten months old in which the blood had all the characteristics of pernicious anæmia as seen in adults, except that the color index was never high. I examined the blood and predicted the baby would die. It rapidly recovered and has now been well for two years. I know of no case precisely similar. Most of the few reported cases of pernicious anæmia in infancy have shown moderate leucocytosis (as compared with adult blood), a fact which deprives us of one of the means of distinguishing the disease from secondary anæmia. The reports as to nucleated corpuscles very rarely separate normoblasts from megaloblasts, and we have no way, therefore, of being sure on this important point. The high color index and large diameter of the red cells are occasionally seen in other anæmias of infancy and are not always present in pernicious cases. The great fatality of all kinds of anæmia in infancy prevents our calling a case *pernicious* because of a fatal termination. Enlargements of the liver and spleen occur in many cases of each type of infantile anæmia, and occasionally in pernicious anæmia of adults. They do not, therefore, exclude pernicious anæmia in infancy.

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[1] Baginsky: Arch. f. Kinderheilk., 1892, vol. xiii.

[2] Senator: Berlin. klin. Woch., 1892.

[3] Fischl: *Loc. cit.*

[4] Andeoud: Rev. méd. de la Suisse rom., 1894, p. 507.

[5] Monti and Berggrün: *Loc. cit.*

[6] Felsenthal: *Loc. cit.*

[7] Rudnitz: Prag. med. Woch., 1894, p. 6.

[8] Epstein: Prag. med. Woch., 1894, p. 6.

[9] Alt and Weiss: Centralbl. f. med. Wissenschaft, 1892.

[10] Hock and Schlesinger: *Loc. cit.*

[11] Crocq: "Étude sur l'Adénie," etc., Brussels, 1819 (Lamartin).

[12] Rotch: Pædiatrics, 1895, p. 361.

[13] Rotch and Ladd: Pædiatrics, September, 1901.

Bearing these facts in mind, it is evident that some of Luzet's cases of "anæmia infantum pseudoleukæmica" may have been pernicious anæmia. Von Jaksch's own cases may have been either (*a*) Hodgkin's disease with leucocytosis, (*b*) grave secondary anæmia with leucocytosis (Monti and Berggrün), or (*c*) leukæmia.

(*b*) Hodgkin's disease, which v. Limbeck finds to be very common in infancy, may affect the liver and spleen and not the external lymph glands, and may be accompanied by anæmia and leucocytosis such as v. Jaksch describes. Epstein considers that this is the case, and hence denies the existence of any such disease as the anæmia infantum pseudoleukæmica.

(*c*) As any anæmia secondary to rickets or syphilis may or may not have enlarged spleen and liver and marked leucocytosis, we cannot tell from v. Jaksch's description that we are not dealing in his cases with secondary anæmia. The table on pages 522 and 523 from Morse[1] gives a fair sample of cases of anæmia in infancy of various degrees of severity, and shows the lack of any interdependence between splenic tumor, the number of leucocytes of erythrocytes or of megaloblasts, and the prognosis.

(*d*) Since v. Jaksch does not give any accurate differential count of the leucocytes, there may have been large numbers of myelocytes in his cases for all we know, or an overwhelming percentage of lymphocytes, *i.e.*, either type of leukæmia.

One of the cases reported by Rotch as "anæmia infantum pseudoleukæmica" had 80 per cent of lymphocytes in a leucocyte count of 116,500, the ratio of white to red cells being 1: 11, and the nucleated corpuscles abundant. The external lymph glands as well as the liver and spleen were enlarged. How such a case is to be distinguished from lymphatic leukæmia without autopsy I cannot see. Large numbers of nucleated corpuscles with mitoses (present in this case) are to be found in any anæmia of infancy in which the red cells, as in this case, have sunk as low as 1,311,500, and therefore do not exclude leukæmia.

Von Jaksch protests that his cases are not secondary to rickets or any other disease, but Fischl[2] in a careful study of all the pub-

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[1] Morse: Boston Med. and Surg. Jour., May 28th, 1903.

[2] Fischl: Zeit. f. Heilkunde, 1892.

Number.	Spleen.	Liver.	Glands.	Red corpuscles.	Per cent hæmoglobin.	White corpuscles.	Per cent small mononuclear.	Per cent large mononuclear.	Per cent polynuclear neutrophiles.	Per cent eosinophiles.	Per cent myelocytes.	Morphological changes.	Etiology.					Results.
													Rickets.	Syphilis.	Improper food.	Gastro-enteric disorders.	Miscellaneous.	
1	1	4	?	1,250,000	15	10,300	67.0	2.0	29.0	2.0	....	Marked.	*	Yes.	Yes.	Yes.	....	Died in one month.
2	2	N.	*	3,288,000	42	4,800	49.0	5.0	45 0	1.0	....	One normoblast to one macroblast.	*	......	Breast.	Yes.	....	Lost in one month. Probably died.
3	2	N.	*	4,519,000	57	15,900	44.0	3.5	47.0	5.5	....	Slight. Normoblasts.	*	......	Breast.	Yes.	....	Died in seven months.
4	2 × 5	N.	* *	2,296,000	25	16,850	4.4	19.6	44.4	.4	1.2	Moderate. Six normoblasts to one megaloblast and one microblast.	* *	......	Yes.	Yes.	....	Well in two and one-half years. Spleen not palpable. Liver normal.
5	2 × 4	3	?	5,072,000	65	16,600	40.0	18 0	41.0	1.0	....	Slight.	*	......	Yes.	Yes.	....	Lost. Probably did well.
6	3 × 4	N.	*	1,736,000	25	4,200	69.0	5.0	25.0	1.0	....	Marked.	0	......	Yes.	Yes.	....	Died in one month.
7	3 × 6	N.	*	3,078,000	30	18,520	31.0	4.0	64.0	1.0	....	Marked. Normoblasts.	*	......	Yes.	Yes.	Premature.	Lost in one month. Probably did well.
8	3 × 4	3	*	5,380,000	65	15,625	43.0	2.0	54.0	.5	.5	Slight.	* *	......	?	?	....	Lost in two weeks. Probably did well.
9	3½	N.	*	950,000	19	27,000	52.0	13.0	32.0	.5	2.5	Marked. Twenty-four normoblasts to twenty-one megaloblasts and eight microblasts.	0	......	?	?	Pertussis.	Died in five days.
10	4 × 8	N.	*	5,158,000	68	15,200	51.0	5.0	40.0	4.0	...	Moderate. Occasional normoblast.	* * *	......	Yes.	Yes.	....	Well in six years. Spleen just palpable. Liver normal.
11	4	6	*	5,650,000	75	11,800	32.0	8.0	51.0	9.0	....	Slight.	* *	......	?	?	....	Well in seven months. Spleen not palpable. Liver—4.5 cm. below ribs.
12	Umb.	2	*	3,564,000	60	16,250	31.0	8.0	60.0	1.0	..	Marked. Megaloblasts.	*	......	?	Yes.	....	Alive in eight months. Doing well. Spleen not palpable. Liver normal.
13	Umb.	3	*	5,800,000	?	15,000	43.0	2.0	55.0	....	...	....	* *	......	Breast.	Yes.	....	Died soon. Meningitis.
14	Umb.	3	* * *	2,553,000	55	8,200	44.0	4.0	50.0	1.0	1.0	Moderate.	*	......	Breast.	Yes.	....	Well in six months. Spleen? Liver?

Number.	Spleen.	Liver.	Glands.	Red corpuscles.	Per cent hæmoglobin.	White corpuscles.	Per cent small mononuclear.	Per cent large mononuclear.	Per cent polynuclear neutrophiles.	Per cent eosinophiles.	Per cent myelocytes.	Morphological changes.	Etiology.					Results.
													Rickets.	Syphilis.	Improper food.	Gastro-enteric disorders.	Miscellaneous.	
15	Umb.	5	* * *	4,340,000	60	31,500	29.5	9.9	56.5	.3	3.8	Very marked. Eleven normoblasts to eighty-nine macroblasts. Nuclear figures.	*	.....	Yes.	Yes.	... .	Died in two months.
16	Umb.	5	*	4,408,000	58	47,220	36.5	9.5	50.5	1.0	2.5	Moderate. Thirteen normoblasts to eighteen macroblasts and one microblast.	* * *	......	Yes.	Yes.	... .	Lost. Probably died.
17	Umb.	6	* *	4,200,000	65	13,400	42.0	11.0	45.0	2.0	....	Moderate...............	*	Yes.	Yes.	Yes.	....	Lost. Probably recovered.
18	A. S. S.	N.	?	3,556,000	60	12,400	28.0	10.0	55.0	7.0	....	Moderate. Megaloblasts most numerous.	* *	......	Yes.	Yes.	....	Well in seven years. Spleen? Liver?
19	A. S. S.	3	*	4,000,000	40	18,750	34.4	12.6	51.0	.2	1.8	Marked. Sixteen normoblasts to nine megaloblasts.	* * *	......	Yes.	Yes.	....	Well in eighteen mos. Spleen not palpable. Liver—3 cm. below ribs.
20	A. S. S.	5	* *	3,750,000	55	16,200	50.0	6.0	39.0	5.0	. .	Slight	*	Yes.	Yes.	?	....	Lost in two weeks. Probably recovered.
21	A. S. S.	* * *	*	3,720,000	65	10,700	30.0	4.0	65.0	1.0	....	Slight	*	......	Yes.	Yes.	....	Well in seven months. Spleen not palpable. Liver—3 cm. below ribs.
22	A. S. S.	3	*	3,750,000	50	29,600	30.0	18.0	48.0	2.0	1.0	Marked. Eight normoblasts to twelve macroblasts and seven microblasts.	* *	......	Yes.	?	....	Died in three days.

* = slight; ** moderate *** = marked.

The figures in the first column mean the length and breadth of the area of spleen exposed below the ribs expressed in centimetres. "Umb." means that the spleen reached to the umbilicus, and A. S. S. that it reached the anterior superior spine of the ilium. In the second column the width of the portion of liver exposed below the ribs is expressed in centimetres. "N" = normal.

lished cases finds that out of a total of eighteen cases sixteen had severe rickets and two hereditary syphilis.

The writings of Raudnitz, Ebstein, Felsenthal, Fischl, and v. Limbeck, which deny the separate existence of the anæmia infantum pseudoleukæmica, are convincing to me, and are reinforced by the few cases of bad anæmia in children which I have seen. We must try to distribute the cases of anæmia with leucocytosis and large spleen under pernicious anæmia, secondary anæmia, and leukæmia. But our problem is not yet nearly solved. All we have gained is the belief that v. Jaksch's new disease does *not* help us to classify these doubtful cases. The difficulty is still very great. The following cases, reported by Dr. Vickery in the *Medical News* for December, 1897, illustrate this:

Case I.—A male child of sixteen months with symptoms of grave anæmia, greatly enlarged spleen and slightly enlarged liver, showed the following figures: Red cells, 2,500,000; white cells, 22,000. Differential count of 500 cells showed: Lymphocytes, 53.8 per cent (46.2 of the smaller type); polymorphonuclear cells, 29.4 per cent; eosinophiles, 6.2 per cent; myelocytes, 10 per cent.

While counting these, 147 nucleated red corpuscles were seen, of which 21 were normoblasts, 50 megaloblasts, and 47 microblasts; 6 showed mitosis in their nuclei.

The child died shortly after without any complication or intercurrent disease. No autopsy. No evidence of rickets or syphilis or other previous disease.

Case II.—Young infant with enlarged external lymph glands and very large spleen. July 14th, 1897—Red cells, 4,300,000; white cells, 31,000; hæmoglobin, 60 per cent; polymorphonuclear neutrophiles, 57.5 per cent; small lymphocytes, 26 per cent; large lymphocytes, 15 per cent; eosinophiles, 0.5 per cent; myelocytes, 1 per cent.

One or two nucleated red corpuscles in every field. Out of 100 of them 89 were large and 11 small. Many showed mitosis. Polychromatophilic forms numerous. July 19th—Seventen megaloblasts seen while counting 1,000 white cells. Blood is otherwise about the same. The case was lost sight of and not traced.

Now I see no reason for supposing these cases to represent a new type of disease, and yet I cannot feel perfectly safe in classifying them as primary anæmia, secondary anæmia, or leukæmia.

(*a*) Primary or pernicious anæmia should have a lower count of red cells. The percentage of myelocytes in the first case (10 per cent) is higher than in any other case of pernicious anæmia on record, though in one adult case with autopsy I found 9.2 per cent with a leucocytosis of 12,500, or 1,150 myelocytes per cubic millimetre, against 2,200 per cubic millimetre in this case.

(*b*) It is hard to call an anæmia secondary which kills with no complications and when there is no evidence of any disease of which it can be secondary.

(*c*) For splenic myelogenous leukæmia the total leucocyte count and the percentage of myelocytes are very small in either case. Still the leucocyte count may drop very low in leukæmia even without any inflammatory complication. Such a case is reported by Osler, in which the leucocytes fell to 7,500, of which only 300, or four per cent, were myelocytes.

Hayem (*loc. cit.*, p. 864) in a ten-months-old child counted 2,712,500 red and 33,000 white cells, almost the same figures as in the case just quoted.. [Hayem unfortunately gives no differential count, but apparently considers the case leukæmic because of the enormous number of nucleated red cells, many with mitoses.] Morse's case of leukæmia in infancy had 2,900,000 red and 48,000 white cells. Twenty-one and four-tenths per cent of the leucocytes, or about 10,000, were myelocytes. The same abundance of nucleated red cells (some with mitoses) were here present as in Hayem's case, so that there is evidently nothing peculiar in their presence in the disease described by v. Jaksch, as Luzet supposed.

These cases show that leukæmia may at certain periods present just such a blood picture as was present in the above-quoted case, and that the number of leucocytes in the leukæmia of infants may be no greater than that in any anæmia with the leucocytosis so common in children. It seems to me the most natural conclusion to be deduced from these facts is that we meet with cases in infancy *which are apparently intermediate between leukæmia and pernicious anæmia*. I have pointed out elsewhere that there are many points of resemblance between the two diseases. The case of leukæmia reported by Osler showed at one period—the period of remission—a fall in the number of leucocytes and in the percentage of myelocytes till the blood was practically that of pernicious anæmia.

Dr. Rotch's case (above quoted) is another in which the diagnosis seems to lie somewhere intermediate between the two diseases, anæmia and leukæmia. The case which I have quoted above seems to me on the whole nearer to the type of pernicious anæmia than of leukæmia, and Dr. Rotch's nearer to the latter than to the former;

but each is really intermediate, *so far as the blood goes*, between the two diseases. I have no intention of suggesting that the organic lesions in these cases are intermediate between leukæmia and pernicious anæmia. It is simply the blood that is so.

Engel's case, reported in Virchow's *Archiv*, vol. 135, suggests the same thing. He calls the case one of "*pseudo-pernicious anæmia.*" Myelocytes were abundant.

Polymorphous Condition.

This illustrates that "polymorphous" condition of the blood which v. Jaksch supposed to be characteristic of the anæmia infantum pseudoleukæmica. The same thing was very marked in all the bad cases of anæmia which I have seen, including the case above mentioned, and a case of true leukæmia in a girl of eight. The impression one gets from the field of a stained specimen is that *no two white corpuscles are alike*. Every species is subdivided into several sub-varieties and all stages of degeneration are to be seen in each variety. But this is characteristic of any very severe infantile anæmia and not of any single type.

LEUKÆMIA.

In Morse's careful article of August, 1894 (*Boston Med. and Surg. Journal*), twenty cases of leukæmia in infancy are collected. As he rightly says, probably most of these cases were not genuine. Only one of them includes a differential count, and this is in a lymphatic case. Morse's case was at that time the only one of the splenic-myelogenous type on record in which the diagnosis is made reasonably certain by a color analysis. Fischl in 1892 said that there was *no* case on record with a differential count.

A case was seen in 1890 by Dr. F. C. Shattuck, which was apparently acute, the symptoms appearing only six weeks before death. Cover-glass preparations examined by W. S. Thayer showed a ratio of about 1 white to 20 red cells. The differential count[1] showed: Small lymphocytes, 97.9 per cent; large lymphocytes, 0.7 per cent; polynuclear cells, 1.4 per cent; eosinophiles, 0.08 per cent.

The other case reported by Morse has been mentioned above.

Charon and Giratea[2] have recently reported a case in a child of eight with 880,000 red cells, 305,000 white cells, and 39 per cent of hæmoglobin. It was apparently of the myelocyte type. E. Müller thinks that there are about five other (German) cases on record, all of acute leukæmia and all with a similar blood count, though in some the large lymphocytes (without neutrophilic granules) have been described as "myelocytes."

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[1] Reported by Thayer in the Boston Medical and Surgical Journal, 1893, vol. cxxviii., p. 183.

[2] Bull. d. Soc. Roy. d. Sciences Méd., etc., Bruxelles, 1897, No. 7.

Müller[1] has reported with great care three cases of leukæmia, all of them in boys four years old—all apparently acute and of the gastro-intestinal type—*i.e.*, the glands and follicles throughout the whole length of the alimentary tract being the chief seats of infiltration, though the liver and spleen were also enlarged. The counts were as follows:

	CASE I.				CASE II.	CASE III.
	April 30th.	May 1st.	May 2d.	May 3d.		
Red cells	1,508,000	1,684,000	1,362,000	1,232,000	2,290,000	1,308,000
White cells	109,500	93,800	46,000	6,800	206,000	420,000
Hæmoglobin	40%	....	....	Death.	25%	
Polymorphonuclear neutrophiles	2%			Many.	1%	.7
Small lymphocytes[2]	85% (8–10 μ diameter).			Few.	15%	2.
Large lymphocytes	13%			Few.	84%	97.3
Eosinophiles	....			Many.	....	.01
Normoblasts	Few.				Two normoblasts seen in counting 1,135 leucocytes.	Seven seen in counting 1,118 leucocytes.
Megaloblasts	Few.					

Since these reports a considerable number of cases of *lymphatic* leukæmia in infancy have been published—some of them acute and not differing markedly from those which occur in adults. *Myelogenous* or mixed-cell leukæmia appears to be rare in infancy. Only a few cases are on record so far as I am aware.

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[1] Jahrbuch für Kinderheilk., 1896, vol. xliii.

[2] All with large pale nuclei.

PART VII.

EXAMINATION OF THE SERUM.

CHAPTER XV.

In a summary of recent literature on serum reactions—a summary which is a model of concise and lucid statement—Sailer[1] has distinguished fourteen types of serum reaction, under each of which numerous sub-types can be recognized. Sailer's list is as follows:

1. Reactions between the *micro-organisms* producing infection and the serum of the infected subject (*e.g.*, between typhoid bacilli and typhoid serum).	1. Agglutination (Widal's reaction). 2. Solution or *lysis* (Pfeiffer's phenomenon). 3. Formation of long skeins of tangled bacilli. 4. Formation of a precipitate in germ-free, filtered cultures on addition of the corresponding serum.
2. Reactions between the *red corpuscles* of some animal and the serum of an animal protected specifically against them (naturally or artificially).	5. Agglutination (clumping). 6. Solution (hæmolysis). 7. Formation of a precipitate when the sera of the two animals (the attacking and the attacked) are mixed.
3. Reactions between the *normal serum* of various animals and different species of *micro-organisms.*	8. Agglutination (clumping). 9. Solution (lysis).
4. Reactions between the *normal or pathological serum* of some animal and the *red corpuscles* of the same or some other animal.	10. Solution (autolysis, isolysis, and heterolysis). 11. Agglutination (rouleaux formation is probably a variety of auto-agglutination).

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[1] Sailer: Univ. of Penn. Med. Bull., August to September, 1902.

5. Reactions between some species of *body cell* (liver cells, leucocytes, spermatozoa, etc.) and the sera of animals immunized against *that cell.*	12. Agglutination. 13. Solution (hepatolysis, leucolysis, spermatolysis, etc.).
6. Reactions between red cells and bacterial cultures.	14. Solution.

To these might be added the reactions between cellular products, such as milk or egg albumen, and the serum of an animal "immunized" against them (*i.e.*, previously injected with milk or egg albumen).

Any attempt to discuss these topics (which are I think the most vitally interesting and important in medicine to-day) would lead far beyond the limits of this book. But it is well, I think, to note that the particular types of serum reaction which we use in diagnosis to-day (the first two of the above list) have their place among a number of other types of serum reactions, any of which may in the near future become of value in clinical diagnosis.

THE WIDAL REACTION IN TYPHOID FEVER.

GENERAL DESCRIPTION.

Although the phenomenon of agglutination is to be obtained in various infections, natural as well as experimental, and with various cells and body fluids, I shall describe as a typical case of it the reaction which may take place when the serum of a patient ill with typhoid fever is added in certain proportions (*vide infra*) to a young bouillon culture of well-certified and virulent typhoid bacilli. In a drop of such a mixture, examined between slide and cover glass[1] with a magnification of 300 diameters or more, we notice at once or within thirty minutes a marked slowing of the progressive movements of the bacilli *or* an unequal distribution of them in the different parts of the preparation. Whichever of these changes occur first, the slowing of locomotion or the tendency to grouping, the other soon follows, and then both processes go on together, as admirably described by Biggs and Park:[2]

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[1] Hanging-drop preparations are often recommended, but a simple slide and cover glass are as good for the purposes of this reaction.

[2] American Journal of the Medical Sciences, March, 1897.

"Some of the bacilli soon cease all progressive movement, and it will be seen that they are gathering together in small groups of two or more, the individual bacilli being still somewhat separated from each other Gradually they close up the spaces between them and clumps are formed According to the completeness of the reaction, either all the bacilli may finally become clumped and immobolized or only a small portion of them, the rest remaining freely motile, and even those clumped may appear to be struggling for freedom. With blood containing a large amount of the agglutinating substances all gradations in the intensity of the reaction may be observed, from those shown in a marked and immediate reaction to those appearing in a late and indefinite one, by simply varying the proportion of blood added to the culture fluid" (see Figs. 47, 48, and 49).

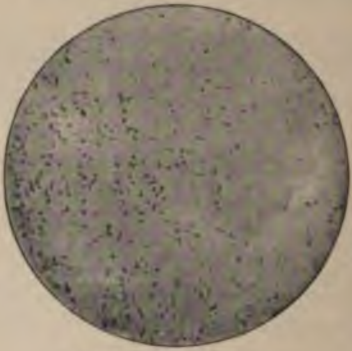

FIG. 47.—Pure Culture.

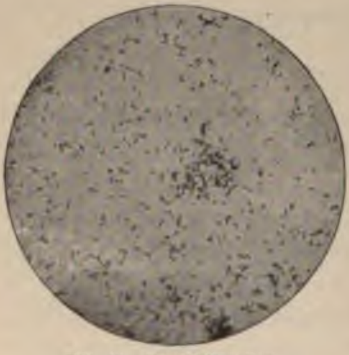

FIG. 48.—Partial Reaction.

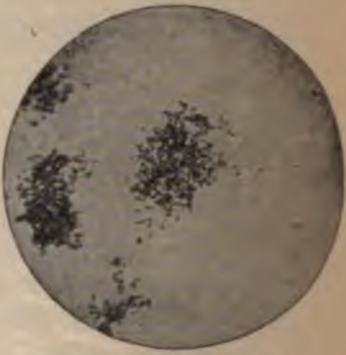

FIG. 49.—Typical Clumping.

The groups or clumps above described constitute the important part of the reaction for diagnostic purposes Of the loss of motility more will be said later.

TECHNIQUE OF THE CLUMP REACTION IN TYPHOID FEVER.

Our account of the methods of obtaining the clump reaction may be divided into the following parts:

1. The body fluids to be used and the methods of obtaining them.
2. The cultures.
3. Dilution and the time limit.

1. THE BODY FLUIDS TO BE USED.

Experiments have proved that the reaction can be obtained with the following fluids:

(*a*) The whole blood, fluid or dried.

(*b*) The plasma and serum, fluid or dried.

(*c*) Also blister fluid, the fluid contents of normal serous cavities, breast milk, pus, tears, and other body fluids.

Of all these fluids, the blood, or the serum, fresh or dried blisters are the only ones used in clinical work.

1. *Use of the Whole Blood—Fluid.*

The advantages of this method are (*a*) its quickness, and (*b*) the small amount of blood (*one drop*) sufficient for the test.

I have used this method in most of my cases and always found it satisfactory and convenient.

Procedure.—Suck up some water with a medicine-dropper and expel ten drops of it into a watch glass. Then empty and dry the dropper, draw up from the watch glass the ten drops just expelled, and mark with a file on the side of the dropper the point up to which the ten-drop column extends. Mark also the point to which one drop (expelled and then sucked up again as before) will rise.

Ten drops of the bouillon culture of the bacilli to be used are then expelled into each of several small test tubes, and one of these tubes is carried to the bedside. After pricking the ear as if for blood examination[1] (see page 7), put the end of the medicine-dropper into the blood drop, and carefully draw back the rubber bulb (which has been previously pushed down over the glass part of the dropper) until the blood rises to the mark for one drop. Wipe from the outside of the dropper any blood that may adhere there and then expel the drop into one of the little test tubes containing the ten drops of bouillon culture. In this way blood can be taken for examination from a dozen patients in as many minutes.

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[1] Squeezing and milking the ear are of no harm in this procedure and enable us to get on with a trifling and painless puncture.

2. *Whole Blood—Dried.*

The advantages of the method are (*a*) the ease and quickness with which the blood can be obtained, (*b*) the convenience for transportation by mail, and (*c*) that it does not deteriorate or become contaminated by bacterial growth, as specimens of fluid blood or serum are so apt to do. Its clumping power is fully equal to that of the serum *in most cases*.[1]

Procedure.—The blood should be dried either upon a glass slide or on a piece of glazed paper or card. Any absorbent substance is less available. Glass is easier to sterilize than paper. Several large drops should be placed in different parts of the glass or paper and *thoroughly* dried.

If paper has been used, we cut out the dried blood drop with a pair of scissors, keeping close to the blood all round, and drop it into a test tube containing one or two drops of water, in which with some sharp-pointed instrument we mix the dried blood, freeing it as well as possible from the paper.

To the liquid so obtained add eight or nine drops of the bouillon culture of bacilli and proceed in the ordinary way. Or we may drop the fragment of paper holding the blood directly into ten drops of bouillon culture—using the bouillon itself to soak off the blood from the paper.[2]

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[1] Widal and Delépine think the fluid serum is slightly more powerful than the dried blood. Johnson admits that in one-tenth of the cases the serum is the more powerful. I have obtained reactions with the dried blood in only seven-eighths of the cases in which I got them with the fluid serum.

[2] Some observers gather the blood on a bit of tinfoil and later crack it off, and after weighing it can make exact dilutions. Or we may soak blood into bits of filter paper of standard size and porosity and thus acquire a known amount as a basis for exact dilutions.

The Fluid Serum.

The ear is pricked in the ordinary way and about twenty drops are forced out by strong squeezing. The blood is received in a small (preferably two-inch) test tube.

The blood when collected may be at once centrifugalized, and the plasma used for the test, or we may wait till clotting occurs and use the serum. When blood is collected in test tubes, it is convenient to free the edges of the clot from the tube all round with some sharp instrument, so that the serum may not be pinned down underneath the clot, as it often is. If this is done, a drop of serum can be had within two or three minutes, and is then mixed with ten drops of bouillon culture, as above described, and examined at once between slide and cover glass.

(Dried serum can be used in the same way as dried blood, but has no special advantages and has not been frequently employed by any observer.)

2. THE CULTURES OF TYPHOID BACILLI TO BE USED.

1. The stock cultures grow best on agar at room temperature.
2. Ordinary peptone bouillon, free from sediment, is the best medium for the test culture. It should be just on the verge of litmus acidity, giving no blue to the red paper and requiring 3 5 per cent of normal alkali to render it neutral to phenolphthalein.
3. The cultures should be *young*—that is, the transplantation to bouillon should have taken place not more than from twelve to twenty-four hours before the culture is used.
4. The virulence and motility of the culture are very important. Most observers agree that the more virulent the culture the more readily and characteristically it is clumped by typhoid serum. Biggs and Park noticed that one culture of peculiarly great virulence recently received from Pfeiffer of Berlin worked much better in their cases than any other of the cultures used.

Cultures fresh from an autopsy usually show *furious* motility, the bacilli darting about like a swarm of insects, but after repeated transplantations and long sojourn in the thermostat a good deal of this motility is gradually lost. *Cultures kept at room temperature preserve their motility for much longer periods.*

For those who have no opportunity to test the virulence of organisms on animals, the motility is the best guide to virulence, and

the rule should be: *Among the available cultures select that having the most rapid motility*.

4. Certain cultures contain small clumps of bacilli *before any serum has been added to them*. This is a very important point and has doubtless misled many. In consequence of this possibility every culture must be examined *each time* that a test is made.

It is hardly necessary to say that the cultures used must have been submitted to all the regular tests for the recognition of the typhoid bacillus, and that the greatest care must be used to avoid their contamination.

The Use of Suspensions or Emulsions of the Bacilli instead of Cultures.

A few observers—particularly Durham and Grüber—have preferred to use a mixture of small bits of solid agar culture and bouillon instead of bouillon cultures. The majority of writers prefer cultures.

The Use of Attenuated Cultures.

Johnson found that with his methods of technique (dried blood and no definite dilution) pseudo-reactions were not uncommon with the blood of healthy people.

He avoids this by using attenuated cultures—*i.e.*, old stock agar cultures kept at room temperature and not transplanted more than once a month, from which he planted his bouillon cultures. This gives a bacillus of reduced virulence and slow, gliding motion, which is clumped far less readily than the virulent varieties. Bouillon cultures of this kind from twelve to twenty-four hours old he found to react in fifteen minutes with all typhoid sera and not with other sera even after forty-eight hours' waiting.

3. DILUTION AND THE TIME LIMIT.

1. *Dilution.*

I have mentioned without explanation in various parts of this chapter that the blood serum or other fluids used must be diluted with at least ten times their volume of bouillon culture before any observation is made as to their action on the bacilli of typhoid fever. The reasons for this dilution and for the proportions 1: 10 are the following:

It has been found, as mentioned above, that the mere formation of clumps in bouillon cultures of Eberth's bacilli is not a power exclusively possessed by typhoid serum. The serum of persons suffering from other diseases and even of healthy persons will form clumps exactly like those formed by typhoid bacilli, *provided it is not diluted.* The only known peculiarity of the typhoid serum is that its clumping power is *greater* than that of other diseases, and persists in spite of dilution, while the sera of diseases other than typhoid lose their power to clump typhoid bacilli when diluted ten times or more.

2. *Time Limit.*

But even this statement must be further limited. The sera of various other diseases, and of healthy persons, will sometimes clump typhoid bacilli *even in a 1 : 10 dilution, provided we give them time enough.* We must therefore limit the period within which a serum must "come up to the scratch" and do its work, if it is to be considered a typhoid serum.

Following Grüber and Durham, a time limit of *one-half hour* has been adopted by Grünbaum, Block, Haedke, Park, and others, but later research convinces me that a fifteen-minute time limit is safer.

All that these more or less arbitrary figures stand for is this: that *hitherto no one has reported any considerable number of cases in which the serum of any disease or of healthy persons has clumped typhoid bacilli within fifteen minutes, when diluted 1 : 10 and used with unimpeachable technique.*

Microscopical Examination.

An artificial light is preferable. The use of hanging-drop preparations is unnecessary, as a simple slide with a cover glass is satisfactory. A hanging-drop cell may be extemporized by cementing with marine glue a small brass curtain ring to a slide, and inverting the cover glass within it, as advised by Stokes.

I have collected over 8,000 cases of supposed typhoid fever in which the clump reaction was tested as above described either with the fluid or dried blood. Of these, 95 per cent showed a serum reaction at some time in their course; 2,500 odd controls showed about 2 per cent of positive results in cases other than typhoid. Altogether then about 10,500 cases have been tested. If we leave out the reports of those whose experience covers less than 100 cases, we have left 4,339 cases observed by 18 physicians in which the percentage of error is 2 per cent only.

A. C. Abbott[1] reports on 11,825 cases with if not over five per cent between the laboratory and the clinical diagnosis. He uses dried blood.

How early does the reaction appear? Few of the many observers who have written on this point have discussed how the beginning of the disease is settled and what they mean, *e.g.*, by the "fifth day of the disease." It might be dated from the first day of malaise and indisposition, from the nose-bleed or the beginning of headache, or from the time of going to bed.

Allowing for such serious uncertainties as this, we find that while the majority of observers record the sixth to eighth day as the earliest on which the reaction appears, there are quite a number of cases mentioned in which it was seen on the fourth or fifth day; a few record reactions present on the third day, and two or three on the second day.

How late in the disease does the reaction last? The majority of observations agree that in mild cases the reaction may die out even before the end of the fever. On the other hand, the reaction usually lasts several months, and Widal found it still present after one year in three out of twenty-two cases in which he tried it. These three subjects had had very severe cases of typhoid three, seven, and nine years previously. It has been reported present twenty and even thirty years after the fever.

The reaction almost always persists in relapses, even to a second or third relapse, and occasionally it is present *only in relapse and not in the original attack at all.* Biggs and Park record a case in which the diagnosis was proved during the original attack by puncture of the spleen, which showed a pure culture of Eberth's bacilli, yet no serum reaction was present until the second day of the relapse. I have observed several similar cases, and quite frequently not found the reaction until convalescence. The failure to follow up such cases as these accounts for many negative reports.

The Intensity of Reaction.

Widal and Sicard record clumping with a dilution of 1: 12,000 and 1: 1,800 and consider that in the active stages of the disease a dilution of 1:60 or 1:80 does not usually present the reaction, while in convalescence the power of the serum falls off gradually and is not always present even at 1:10.

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[1] Abbott: Phil. Health Board Rep., 1899, 1900, 1901.

Biggs and Park find one-half their typhoid cases furnish serum with the power to clump in 1:40 dilution by the end of the first week, and have occasionally noted the reaction even with a dilution of 1:200.

Control Cases.

Out of over three thousand cases of various diseases not typhoid, not over a dozen have been proved to clump typhoid bacilli with proper technique. It is quite possible that further improvements in technique may enable us to prevent even this very small error.

Summary of Clinical Evidence on the Sero-Diagnosis of Typhoid Fever.

The blood of over ninety-five per cent of all cases of typhoid shows a clumping power in some part of their course, but in at least half the cases this does not appear until the second week of the disease, while in a small number of cases it first appears in relapse or convalescence. The clumping power may disappear before the defervescence and may be present only eight days in all; as a rule it persists from the sixth or eighth day until convalescence is established.

In diseases other than typhoid a clump reaction is very rarely to be obtained, provided a dilution of at least 1:10 is used with a time limit of one-half hour. There is no one disease in which clumping is especially apt to occur.

Clinically the reaction is of considerable value, especially when the diagnosis is in doubt after the first week of the disease.

SERO-DIAGNOSIS OF DISEASES OTHER THAN TYPHOID.

1. *Cholera.*

Grüber and Durham first showed that human cholera serum would clump cholera vibrios, following the researches of Pfeiffer *in vivo* by demonstrating a similar reaction *in vitro.*

Achard and Bensaude have applied this to the actual diagnosis of cholera in man with considerable success. In fourteen cases, thirteen clumped readily; two of these were on the first day of the disease. Thirty control cases were negative. The presence of the pellicle renders it unsafe to use bouillon cultures except such as have no pellicle, for bits of it are much like true clumps. Suspensions of twenty-hour gelatin cultures are more convenient. The dilution and time limit are the same as in typhoid. Some cases will react even in 1:120 dilution. The reaction can be performed with dried blood and persists into convalescence (seven months or more).

2. *Malta Fever.*

Wright and Smith tested the serum of fifteen cases of Malta fever with the *micrococcus melitensis* of Bruce, and found a strong clump reaction to occur (1:50 in most cases). On the typhoid bacillus the serum of these cases had no action. Sixteen cases of typhoid showed no reaction with Bruce's organism. The evidence in favor of this organism as the cause of Malta fever is strengthened by these facts. Wright's observations have been confirmed by Neusser and others in this country.

Curry[1] reports his experience in twenty-six cases. He used suspension of dead cocci from seven-day agar cultures in normal salt solution. One drop of the suspected blood was mixed with thirty of normal salt solution, and this mixture was combined with an equal bulk of the suspension of cocci and left to stand in tubes 7.5 cm. long and 3 or 4 mm. in diameter, the lower end being drawn out to a fine point. Sedimentation occurs in positive cases within twenty-four hours. The negative cases remain turbid for days.

3. *The Bubonic Plague.*

Zabolotny[2] studied forty cases at Bombay in April, 1897, and found the reaction absent in the first week, present in 1:10 dilution in the second week, and in 1:50 dilution in the third or fourth week. He noted that the action of the infected serum seemed to deprive the bacilli of their capsules. In an editorial in the *Arch. Russes de Pathologie*, May 31st, 1897, it is stated that the reaction increases in intensity until the fourth week of the disease and then declines; also that it is most marked in the severest cases. Feindel (*loc. cit.*) states that in the acute pneumonic cases the reaction is absent.

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[1] Jour. of Med. Research, July, 1901.

[2] Deut. med. Woch., 1897, p. 392.

The serum reaction is not often of practical value in the diagnosis of plague, because it is rather late in appearing, and because the diagnosis can usually be made earlier by the microscopical and cultural tests of blood withdrawn dried from a bulb.

TUBERCULOSIS.

(See above, page 288.)

DYSENTERY.

The bacillus originally discovered by Shiga, though identical in most respects with that isolated at Manilla by Flexner, is not the same in its agglutinative reactions, and neither of these strains agrees with the organism obtained by Bassett and Duval[1] in respect to this reaction. Further than this Park[2] has shown that normal serum is capable of agglutinating both the "Manilla" and the "Shiga" strains in considerable dilution, while, on the other hand, Park has isolated a bacillus morphologically close to the colon group, but with agglutinative reactions like those of the "Shiga" strain. A good deal more work will have to be done before the agglutination test for the organism or organisms of acute dysentery are put upon a satisfactory basis for general clinical work.

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[1] Bassett and Duval: Am. Med., 1902, vol. iv., p. 417.

[2] Park: Am. Assn. of Pathol., Washington, May 12th, 1903.

BIBLIOGRAPHY.

IT has seemed to me best to give a list only of the books which I have found most useful, since the general bibliography of the subject is now large enough to form a volume by itself. Most of the larger works here described contain extensive bibliographies—especially that by Ewing.

Text-Books.

1. **Ewing**: "Clinical Pathology of the Blood," Phila., 2d edition, 1903. 8vo, 495 pp. (Lea Bros.). This is the newest book on the blood and the fullest discussion of the theoretical points connected with diseases of the blood. The bibliography and résumé of the work of other observers contained in each section are admirable. The original observations of the writer are contained chiefly in the chapters on malaria and diphtheria. The tone of the book is admirably sane and judicial throughout. The illustrations are poor.

2. **Ehrlich, Lazarus, Pinkus, and v. Noorden** in vol. viii. of Nothnagel's "Specielle Pathologie und Therapie," issued between 1898 and 1901 (Wien, Hölder & Co.) have written a series of articles on anæmia, leukæmia, and chlorosis, which together amount to many pages 8vo. The clinical aspects and therapeutics of the diseases are included. The hæmatology of the book is on the whole inferior to Ewing's, although parts of it, especially v. Noorden's study of chlorosis, are masterly. The articles on anæmia are interesting as they contain Ehrlich's latest utterances. The work is out of date in some respects owing to its characteristically Teutonic ignorance of important work done in England and America, but it is undoubtedly the standard German work on the subject.

3. **Da Costa**: "Clinical Hæmatology," Phila., 1901, 8vo, 474 pages Conveniently arranged, well illustrated, not especially original.

4. **Hayem**: "Du Sang," Paris, 1889, 8vo, 1035 pages (French) This valuable book is the largest that I know of on the subject, and contains a mine of information on the morphology of the blood in health and disease, mostly from the author's own experience, literature being but little referred to. It contains a comparative anatomy of the blood and a long account of blood development. Unfortunately, it is dominated throughout by a theory of blood formation which has never gained acceptance by any other authority. It is very full on the subject of fibrin formation and of chlorosis. The illustrations are excellent. In a later work, "Leçons sur les Maladies du Sang," Paris, 1900, 8vo, 700 pages (Masson et Cie.), Hayem has brought his previous book in a measure up to date, but the "Leçons" are very diffuse and wordy and

contain but a small fraction of the original work for which Hayem's first book was so notable.

5. v. Limbeck: "Grundriss ein. klin. Pathologie des Blutes," Jena, 1896, 8vo, 888 pages (Fischer). The second edition of this book, which appeared in February, 1896, is more than twice the size of the first edition (1892)—a fact illustrating the rapidity of the subject's growth. It is on the whole the best general text-book known to me, being equally full on all parts of the subject, including, for example, technique (which Grawitz omits) and of the chemistry of the blood, which is at present the author's special interest and on which Hayem is meagre. The illustrations are poor and the type is trying to the eyes. The writer shows little personal experience with the morphology and micro-chemistry of the blood, and this is the weakest side of the book. A large part of the book is concerned with the physiology of the blood.

6. Grawitz: "Klinische Pathologie des Blutes," Berlin, 1895, 8vo, 333 pages (Enslin). Issued in April, 1896. This book is largely devoted to the matter indicated by the title and contains no account of blood technique, and only thirty pages on the normal anatomy and physiology of the blood, while two hundred and seventy concern the blood in disease. The arrangement of the book is very clear and helpful. The author's main interests are in the estimation of the dried residue of the blood in various diseased conditions and in the bacteriology of the blood, so that the book is specially full on these topics. The illustrations are poor. Type and paper are excellent.

7. Coles: "The Blood: How to Examine It," etc., London, 1898 (J. and A. Churchill), 8vo. A clear and fairly complete account of the work of others upon the subject. Especially full on technique.

These are the best text-books known to me on the whole subject. Taylor's masterly monograph, entitled "Studies in Leukæmia" and forming part of the volume of "Contributions from the William Pepper Laboratory of Clinical Medicine" (Philadelphia, 1900), contains within its one hundred and seventy-eight quarto pages not merely an unrivalled account of leukæmia but a great deal of important matter on leucocytosis, anæmia, and most other hæmatological topics. It is by far the best study of leukæmia known to me in any language.

Treatises on Special Portions of the Subject.

1. Reinert's "Die Zählung der Blutkörperchen," Leipzig, 1891 (Vogel), 246 pages, is an admirable account of the avoidable and unavoidable errors in blood examination, and the best methods of reducing error to a minimum. A number of careful examinations of the blood in health and in various diseases are also given; and an outline of the scope of blood diagnosis closes the book.

2. Türk's monograph on the "Condition of the Blood in Acute Infectious Disease" is an admirable résumé of German and French literature on the subject, together with a detailed study of fifty-two cases. Published at Wien and Leipzig, 1898 (Braumüller), 347 pages, 8vo.

3. Rieder's "Beiträge zur Kenntniss der Leukocytosis," Leipzig, 1892 (Vogel), 220 pages, is an admirable work in all respects, although now considerably out of date. It shows, as very few of the foregoing treatises do, a practical acquaintance, on the author's part, with the details of blood morphology and microchemistry. A very large number of blood counts in many diseases are recorded.

4. Löwitt's "Studien zur Physiol. und Pathol. des Blutes u. der Lymphe" (Jena, 1892 [Fisher], 8vo, 138 pages) is mostly concerned with experiments on animals and intended to throw light on the theory of leucocytosis. The conclusions of the book have not been generally adopted, though its facts have been mostly verified.

5. Thayer and Hewetson's book, on the "Malarial Fevers of Baltimore," leaves nothing more to be desired in that direction. It is two hundred and fifteen pages long, published by the Johns Hopkins press of Baltimore in 1895. It contains a summary of the literature of the subject, an analysis of six hundred and sixteen new cases, and some admirable colored plates. It is a model of its kind in every respect, and an ideal for others to aim for. Essentially the same material is reorganized in Thayer's "Lectures on the Malarial Fevers," New York, 1899, Appleton.

6. Ehrlich's "Farbenanalytische Untersuchungen" (Berlin, 1891 [Hirschwald], 137 pages) contains nine short essays by Ehrlich and three by his pupils. Considering the reputation of the writer they are at the present day rather disappointing reading, and contain little that is not better expressed elsewhere.

7. Weiss's "Hæmatologische Untersuchungen" (Wien, 1896 [Prochaska] 112 pages, 8vo) contains many valuable studies on various points.

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